US009814886B2

(12) **United States Patent**
Zhou et al.

(10) **Patent No.: US 9,814,886 B2**
(45) **Date of Patent: Nov. 14, 2017**

(54) **DETECTING AND TREATING ELECTROMECHANICAL DISSOCIATION OF THE HEART**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 2205 days.

(21) Appl. No.: **12/697,019**

(22) Filed: **Jan. 29, 2010**

(65) **Prior Publication Data**

US 2010/0198284 A1 Aug. 5, 2010

Related U.S. Application Data

(60) Provisional application No. 61/148,674, filed on Jan. 30, 2009.

(51) **Int. Cl.**
A61N 1/00 (2006.01)
A61N 1/362 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61N 1/3627*** (2013.01); ***A61N 1/36114*** (2013.01); ***A61N 1/3962*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61N 1/3627; A61N 1/36114; A61N 1/3962; A61N 1/0551; A61N 1/36557; A61N 1/36564
(Continued)

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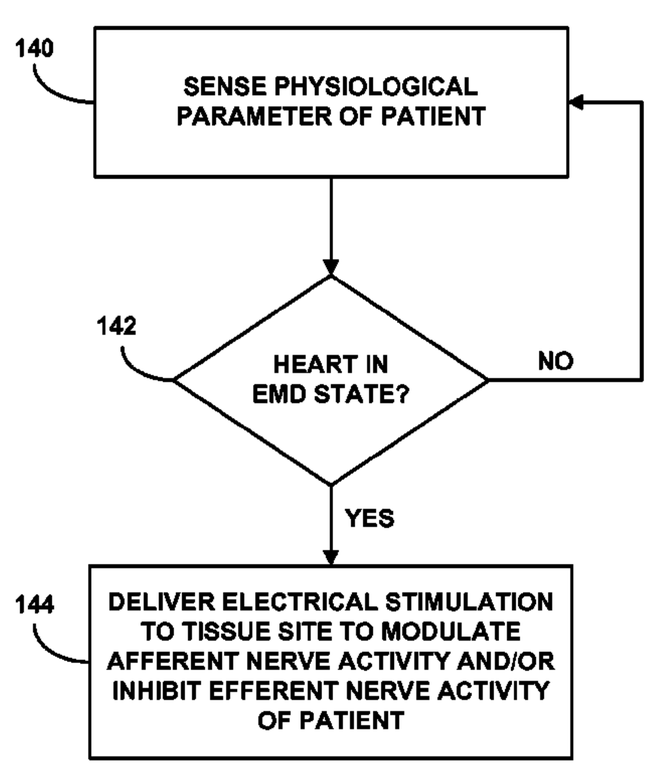
Primary Examiner — Lindsey G Wehrheim

(57) **ABSTRACT**

In some examples, an electromechanical disassociation state (EMD) of a heart of a patient can be treated by delivering electrical stimulation to a tissue site to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in an electromechanical dissociation state, where the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site. The delivery of electrical stimulation may effectively treat the EMD state of the heart, e.g., by enabling effective mechanical contraction of the heart. In another example, an electromechanical disassociation state of a heart of a patient can be treated by determining autonomic nervous system activity associated with a detected EMD state of the heart of a patient, and delivering electrical stimulation therapy to the patient based on the determined autonomic nervous system activity of the patient associated with the EMD state.

27 Claims, 15 Drawing Sheets



(51) **Int. Cl.**

A61N 1/36	(2006.01)
A61N 1/39	(2006.01)
A61N 1/05	(2006.01)
A61N 1/365	(2006.01)

(52) **U.S. Cl.**
CPC *A61N 1/0551* (2013.01); *A61N 1/36557* (2013.01); *A61N 1/36564* (2013.01)

(58) **Field of Classification Search**
USPC 607/4–38, 119–132, 2; 600/373–375, 600/449–450, 481–503, 508–528
See application file for complete search history.

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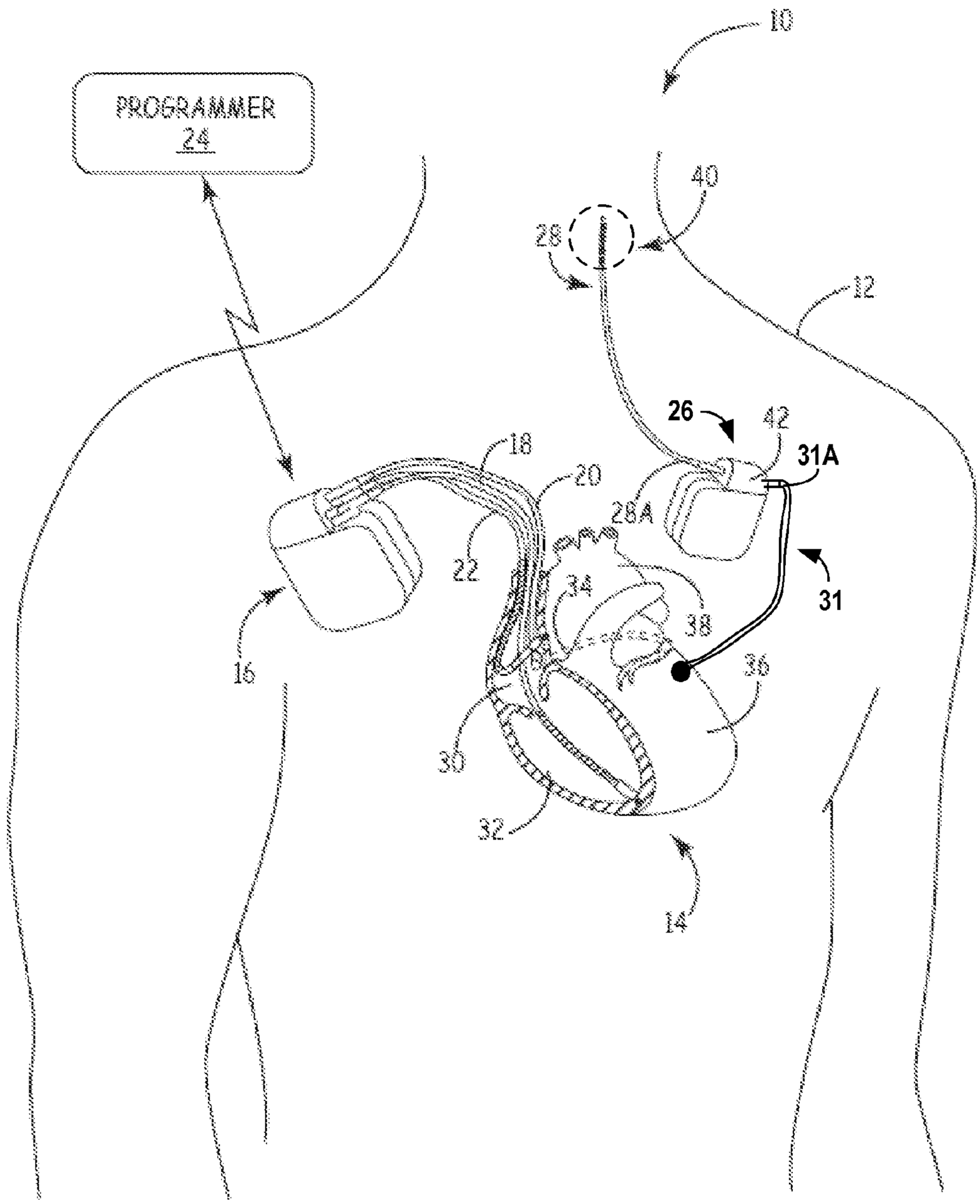
PROGRAMMER
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31A
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28A
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FIG. 1

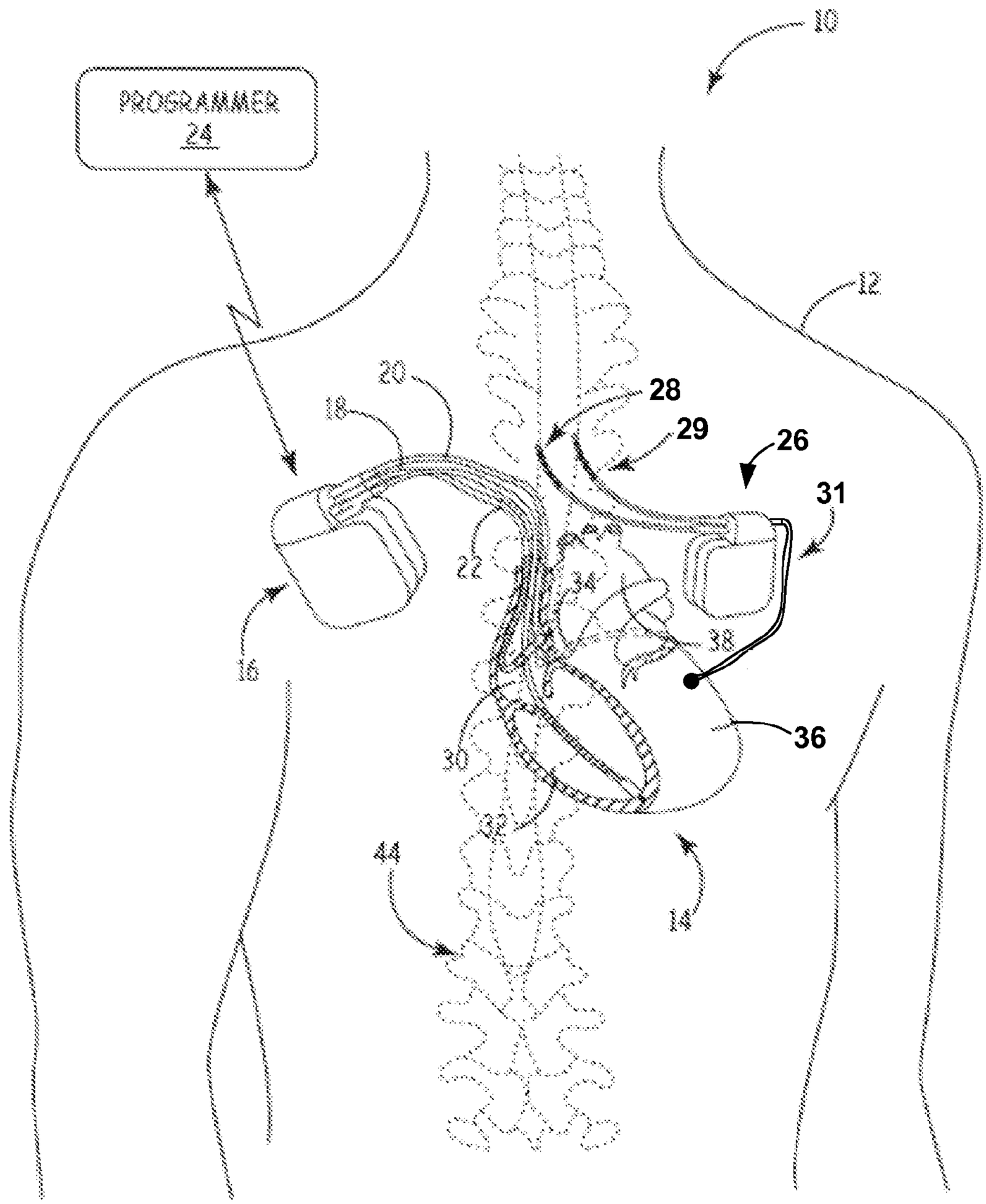

FIG. 2

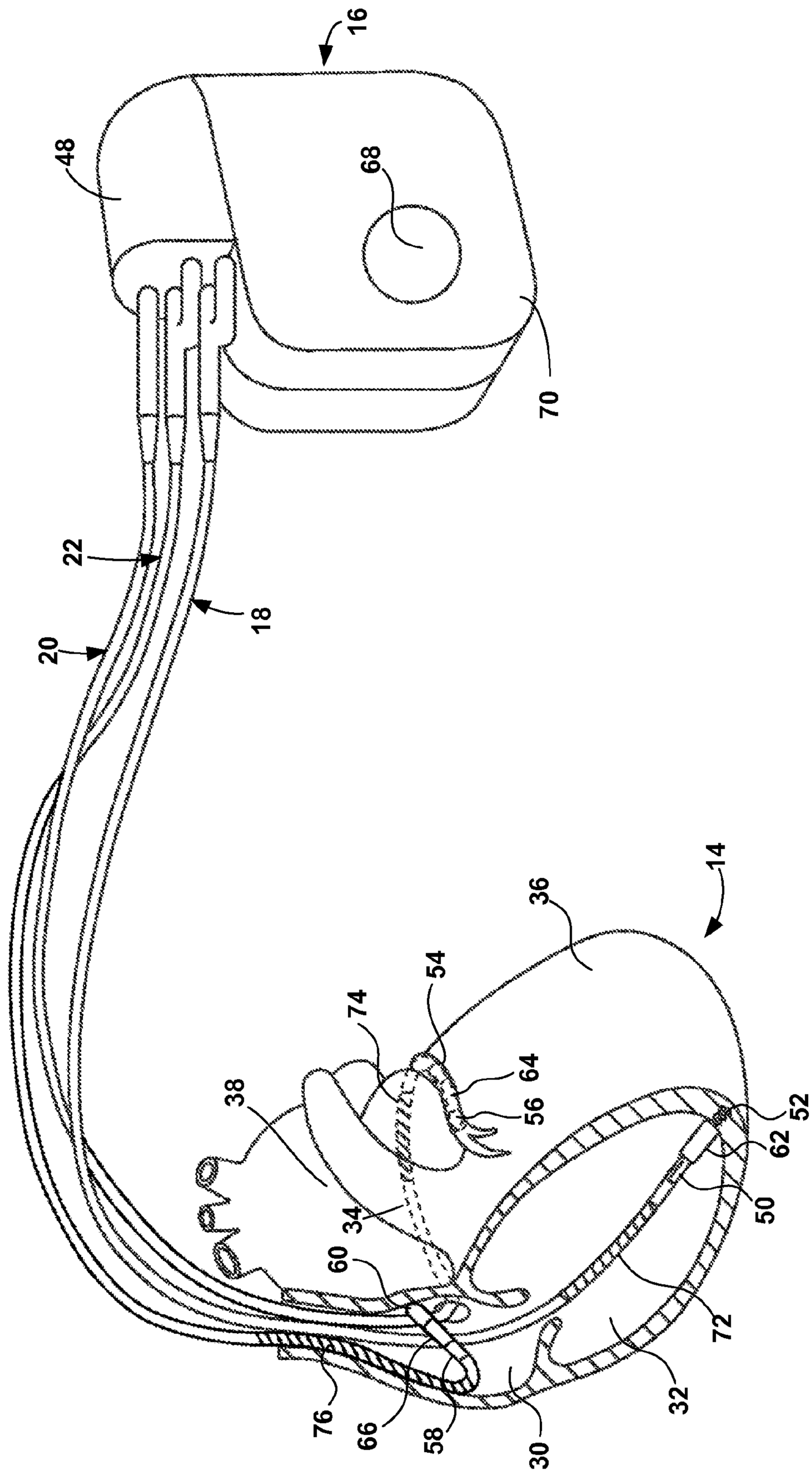
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FIG. 3

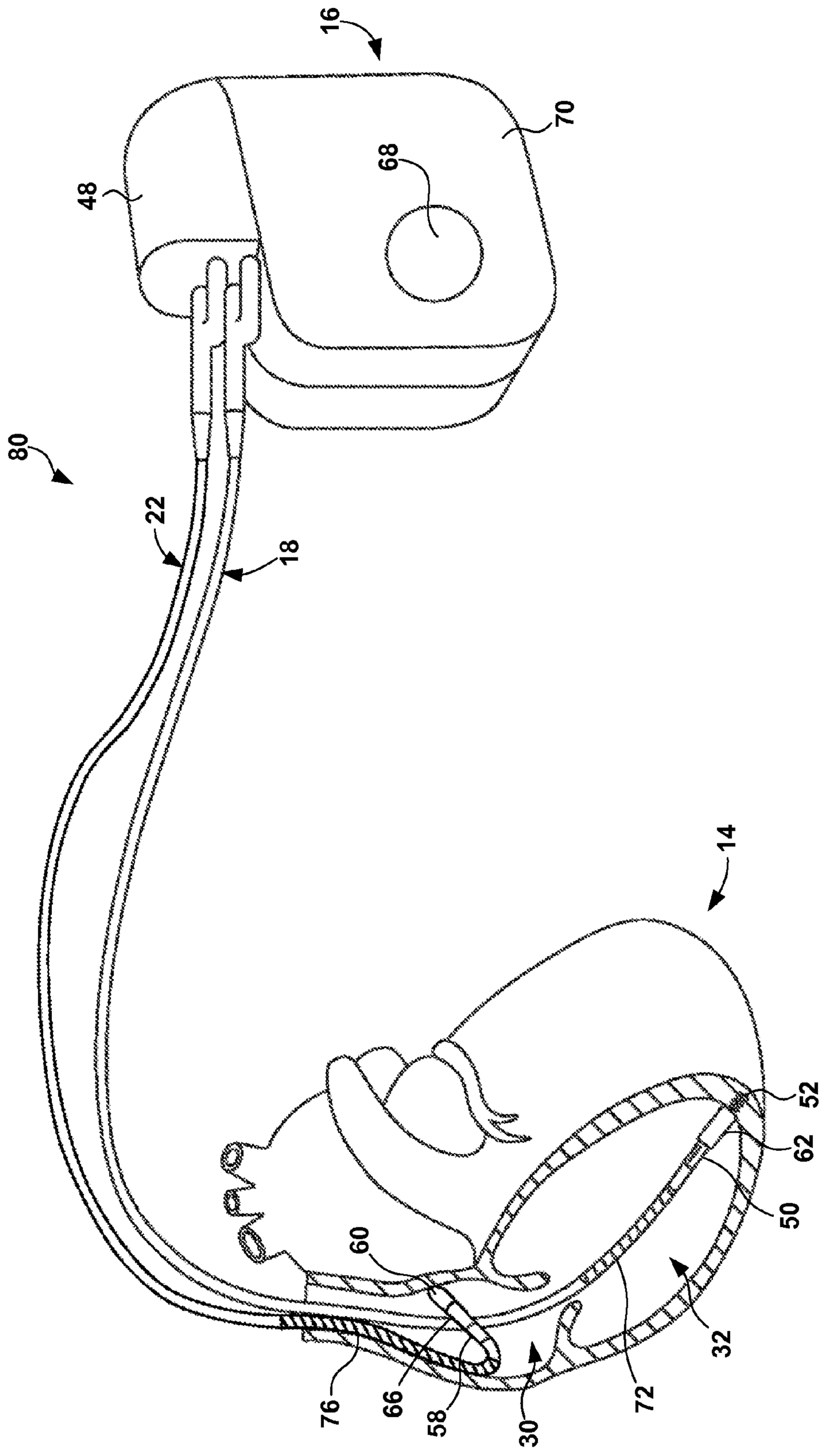


FIG. 4

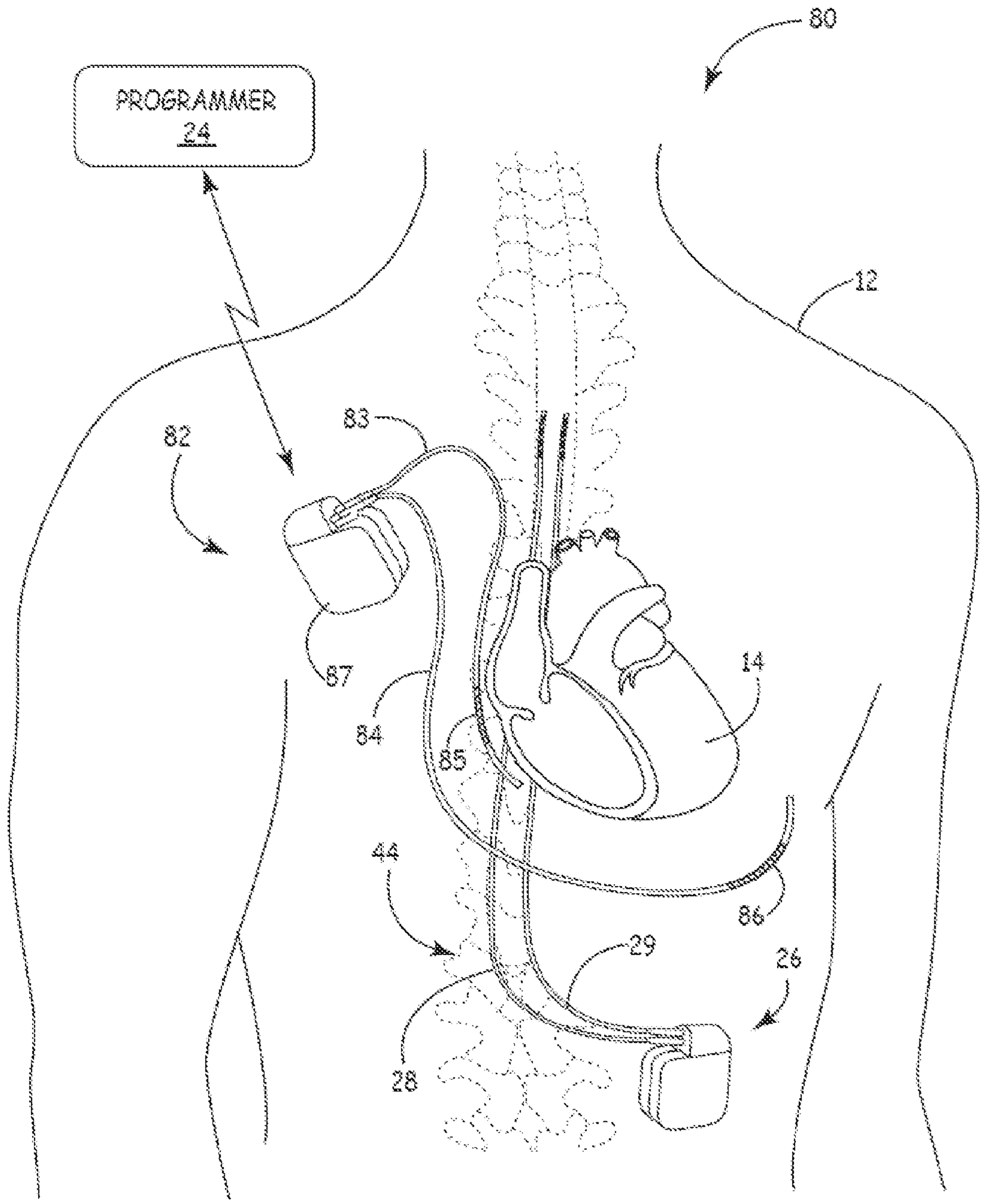
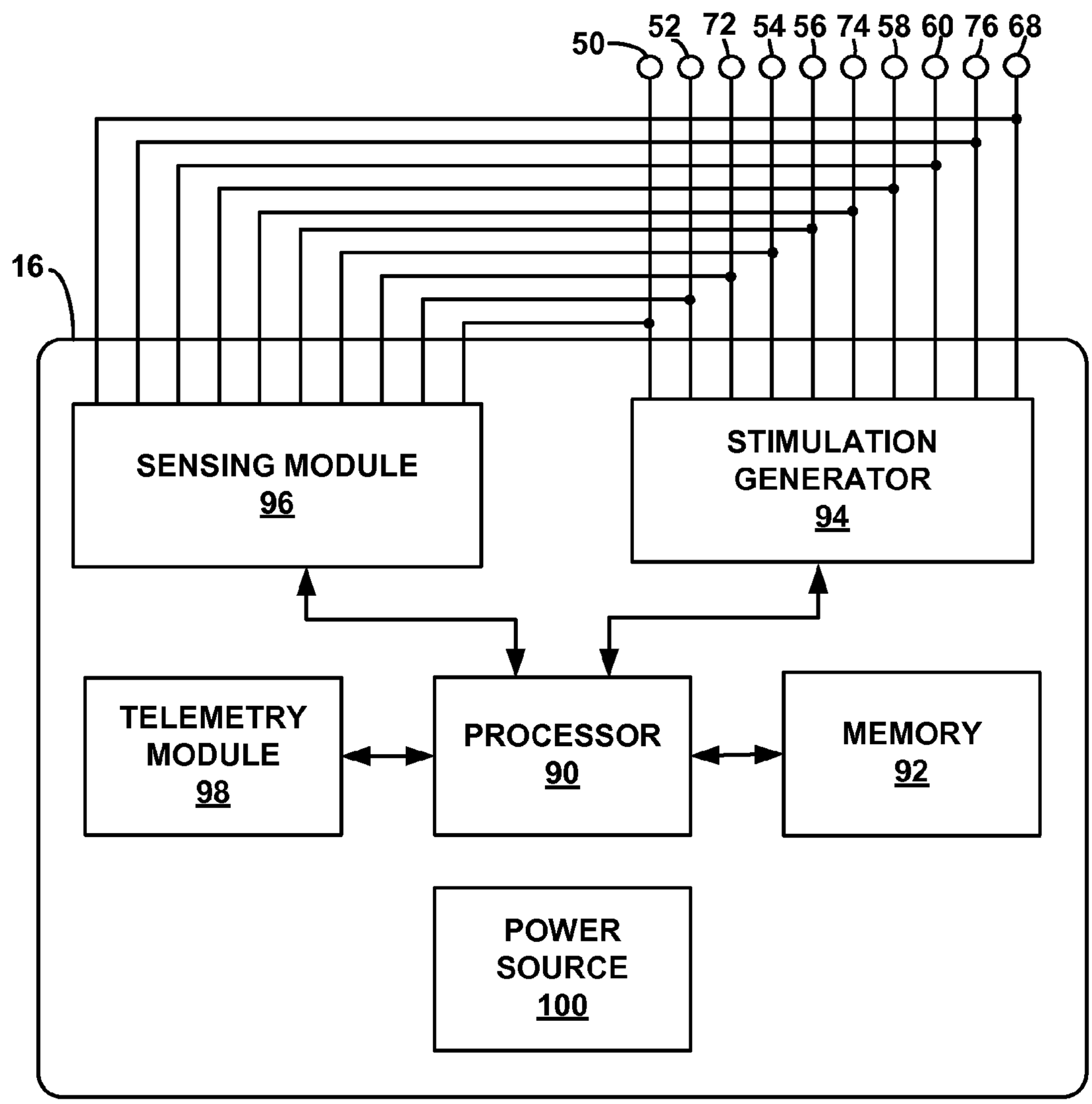


FIG. 5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52
72
54
56
74
58
60
76
68
16
SENSING MODULE
96
STIMULATION GENERATOR
94
TELEMETRY MODULE
98
PROCESSOR
90
MEMORY
92
POWER SOURCE
100

FIG. 6

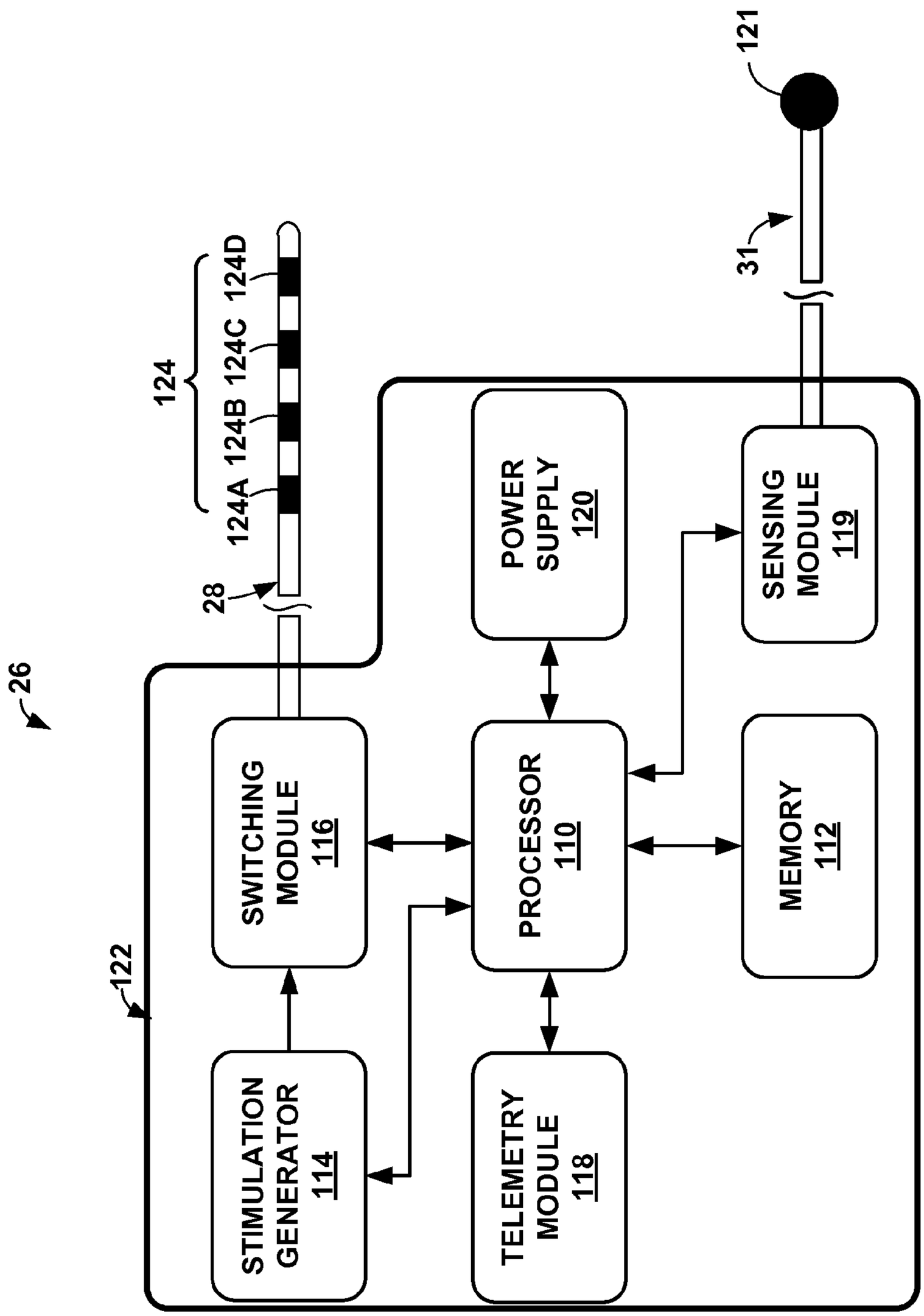
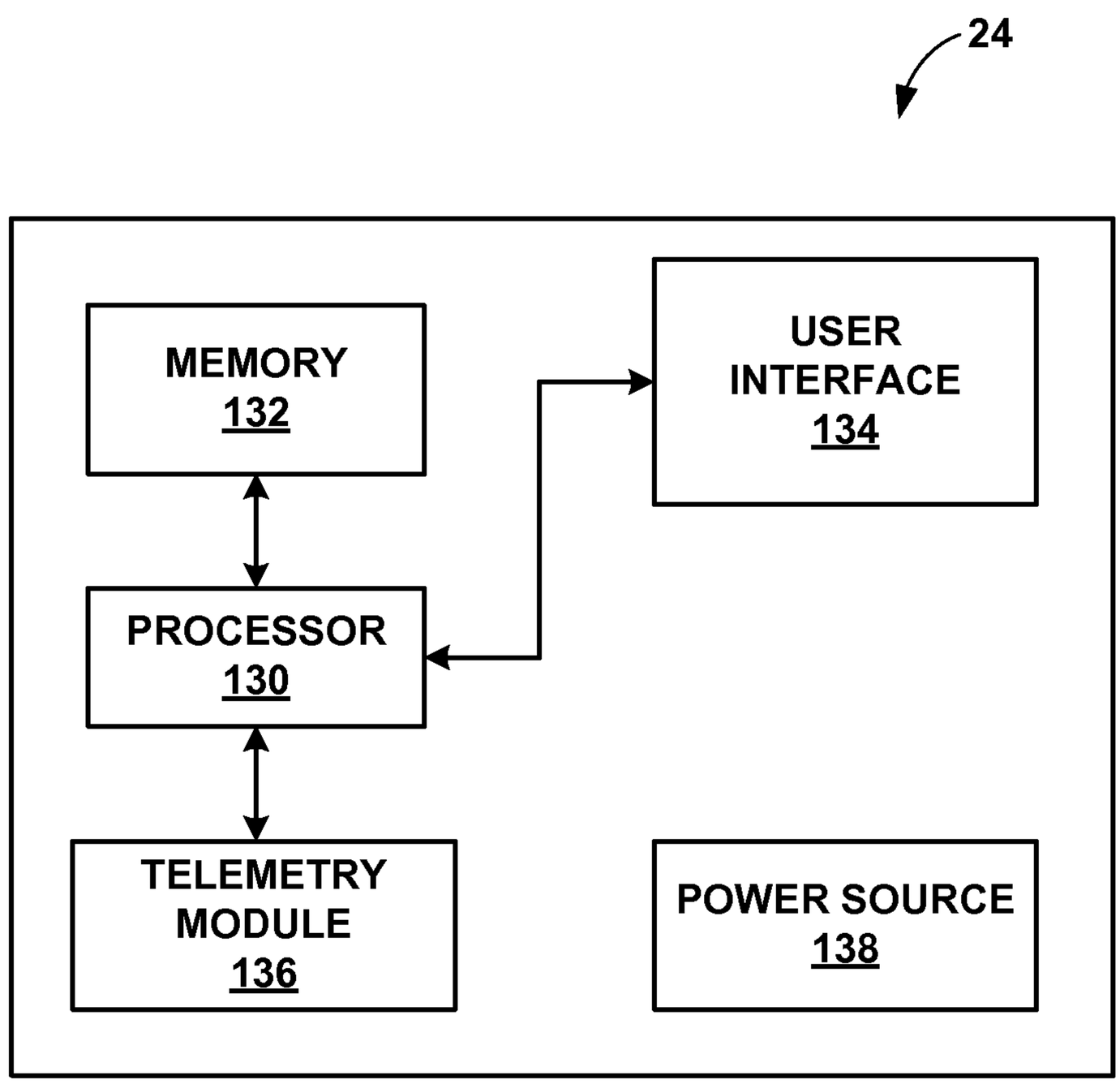

26
122
124
124A
124B
124C
124D
28
121
31
SWITCHING MODULE 116
STIMULATION GENERATOR 114
PROCESSOR 110
TELEMETRY MODULE 118
POWER SUPPLY 120
SENSING MODULE 119
MEMORY 112

FIG. 7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MEMORY
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USER
INTERFACE
134
PROCESSOR
130
TELEMETRY
MODULE
136
POWER SOURCE
138

FIG. 8

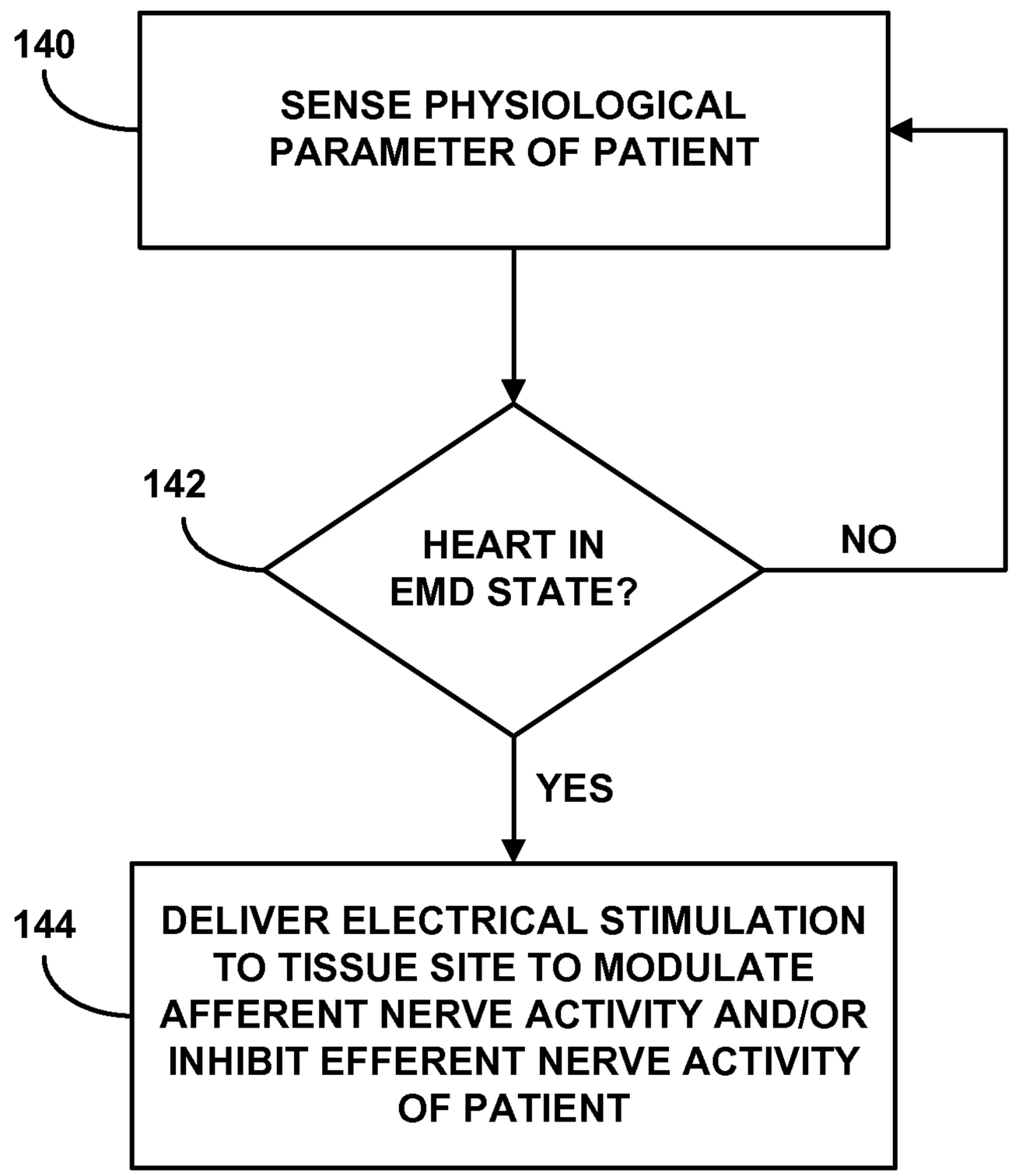
140
SENSE PHYSIOLOGICAL PARAMETER OF PATIENT
142
HEART IN EMD STATE?
NO
YES
144
DELIVER ELECTRICAL STIMULATION TO TISSUE SITE TO MODULATE AFFERENT NERVE ACTIVITY AND/OR INHIBIT EFFERENT NERVE ACTIVITY OF PATIENT

FIG. 9

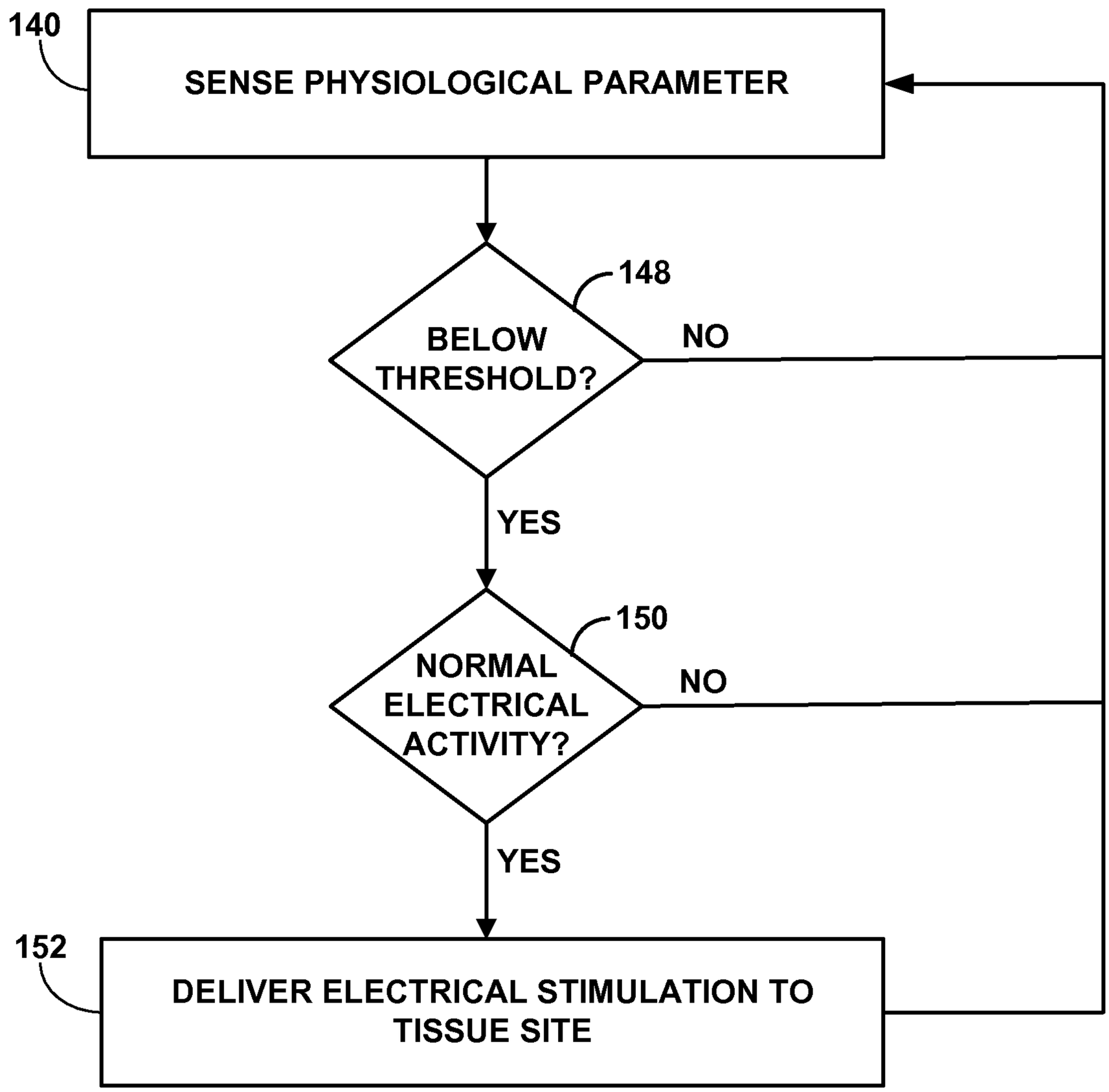
140
SENSE PHYSIOLOGICAL PARAMETER
148
BELOW THRESHOLD?
NO
YES
150
NORMAL ELECTRICAL ACTIVITY?
NO
YES
152
DELIVER ELECTRICAL STIMULATION TO TISSUE SITE

FIG. 10

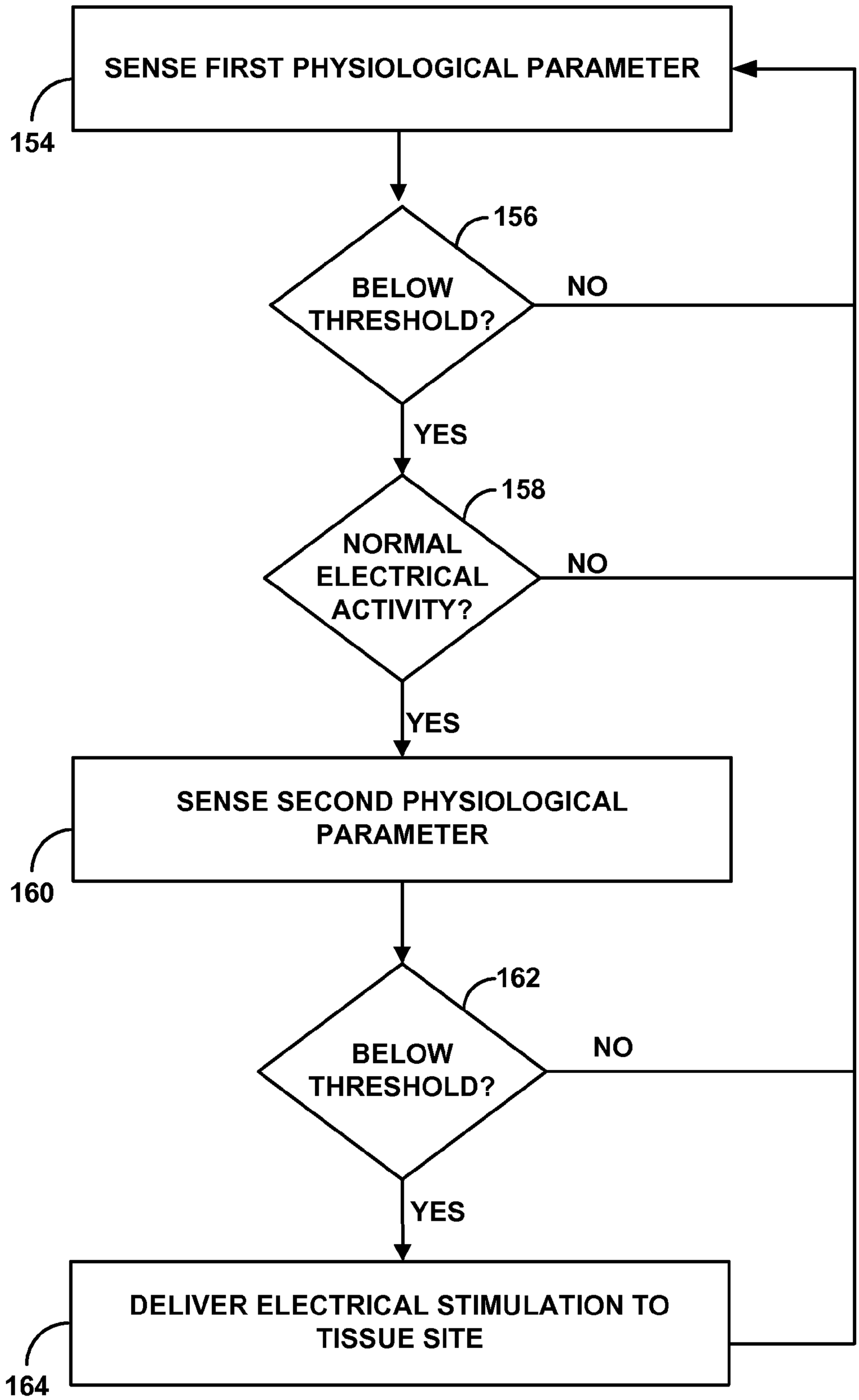
SENSE FIRST PHYSIOLOGICAL PARAMETER
154
156
BELOW THRESHOLD?
NO
YES
158
NORMAL ELECTRICAL ACTIVITY?
NO
YES
SENSE SECOND PHYSIOLOGICAL PARAMETER
160
162
BELOW THRESHOLD?
NO
YES
DELIVER ELECTRICAL STIMULATION TO TISSUE SITE
164

FIG. 11

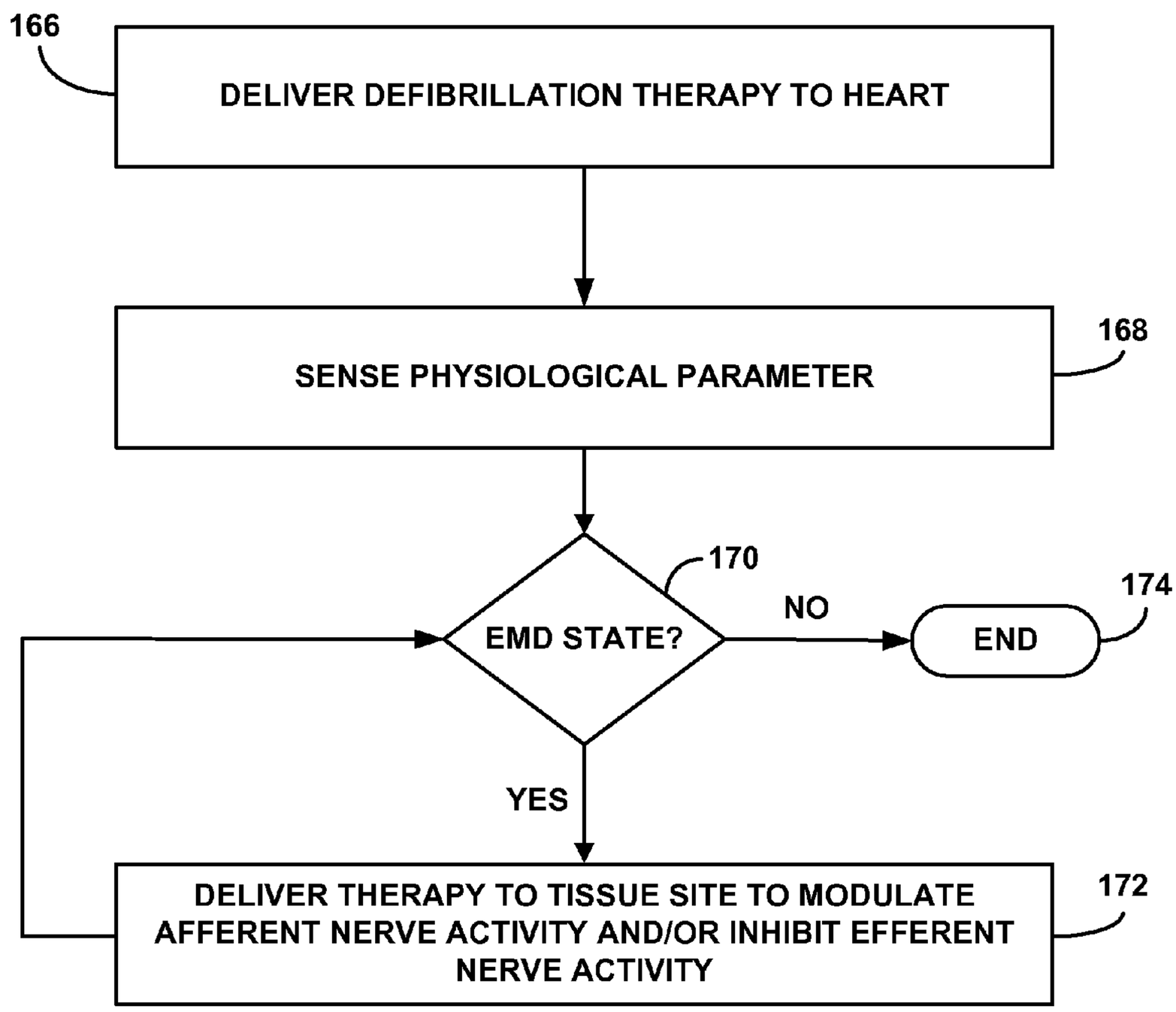
166
DELIVER DEFIBRILLATION THERAPY TO HEART
SENSE PHYSIOLOGICAL PARAMETER
168
170
EMD STATE?
NO
174
END
YES
DELIVER THERAPY TO TISSUE SITE TO MODULATE AFFERENT NERVE ACTIVITY AND/OR INHIBIT EFFERENT NERVE ACTIVITY
172

FIG. 12

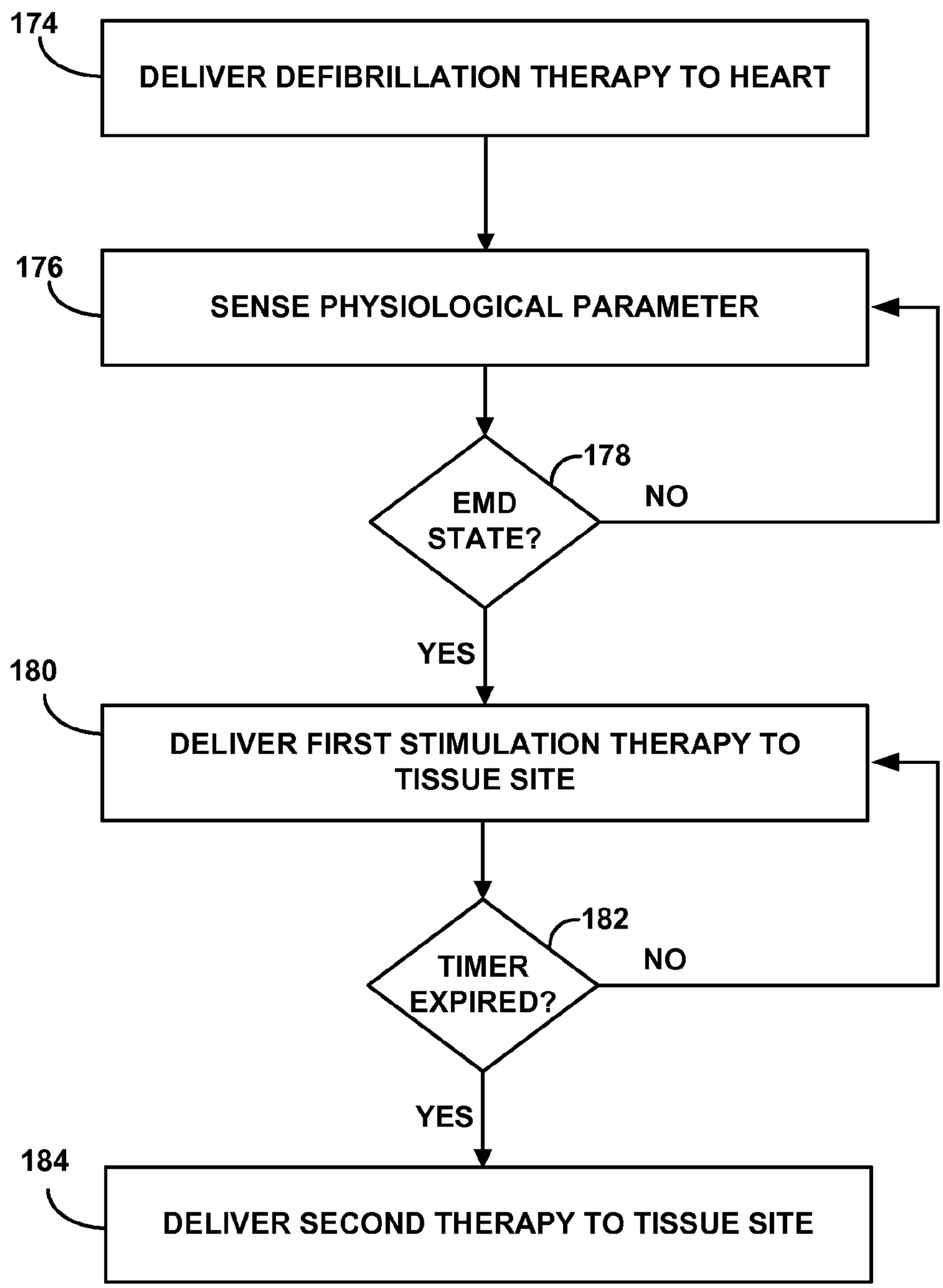
174
DELIVER DEFIBRILLATION THERAPY TO HEART
176
SENSE PHYSIOLOGICAL PARAMETER
178
EMD STATE?
NO
YES
180
DELIVER FIRST STIMULATION THERAPY TO TISSUE SITE
182
TIMER EXPIRED?
NO
YES
184
DELIVER SECOND THERAPY TO TISSUE SITE

FIG. 13

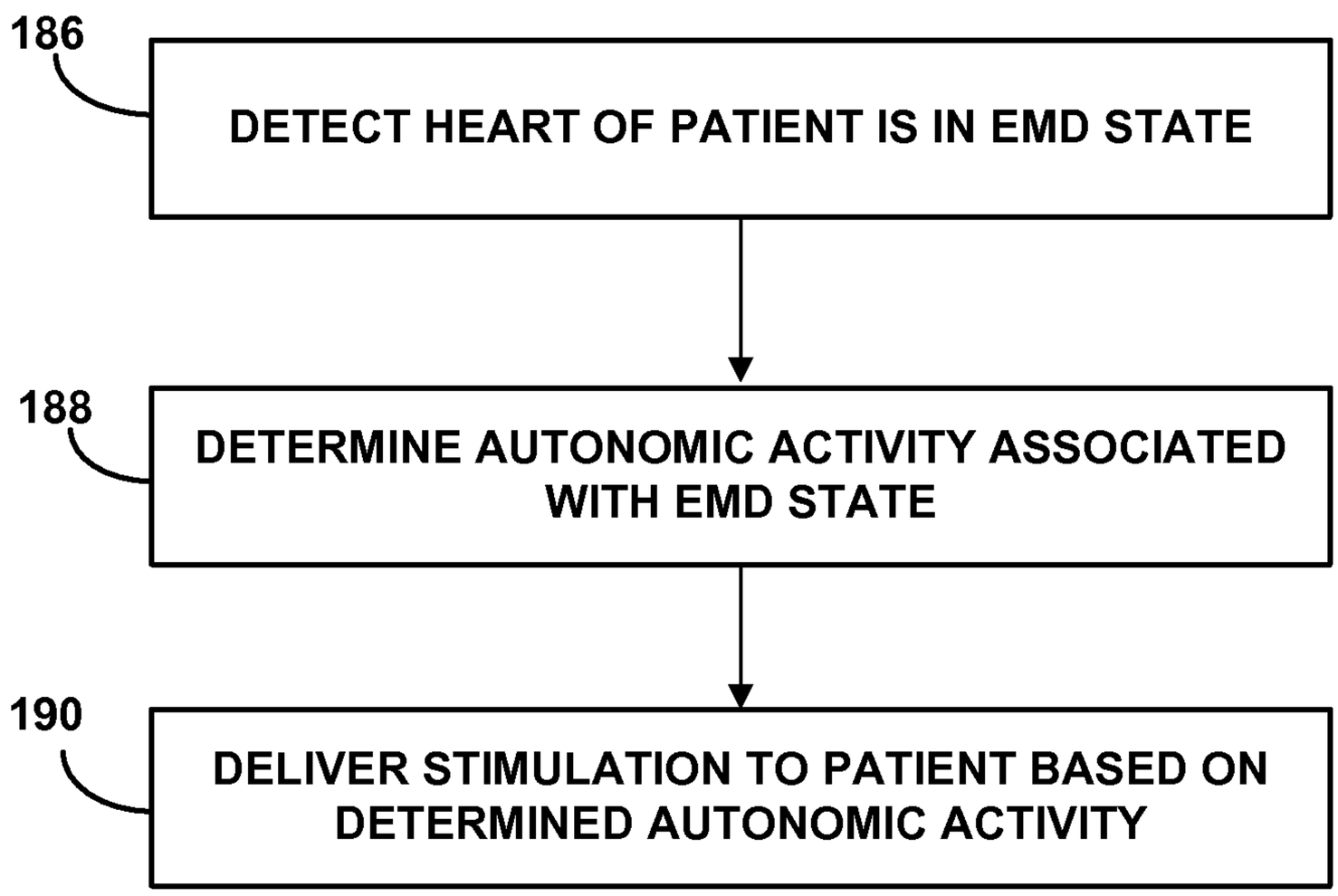
186
DETECT HEART OF PATIENT IS IN EMD STATE
188
DETERMINE AUTONOMIC ACTIVITY ASSOCIATED WITH EMD STATE
190
DELIVER STIMULATION TO PATIENT BASED ON DETERMINED AUTONOMIC ACTIVITY

FIG. 14

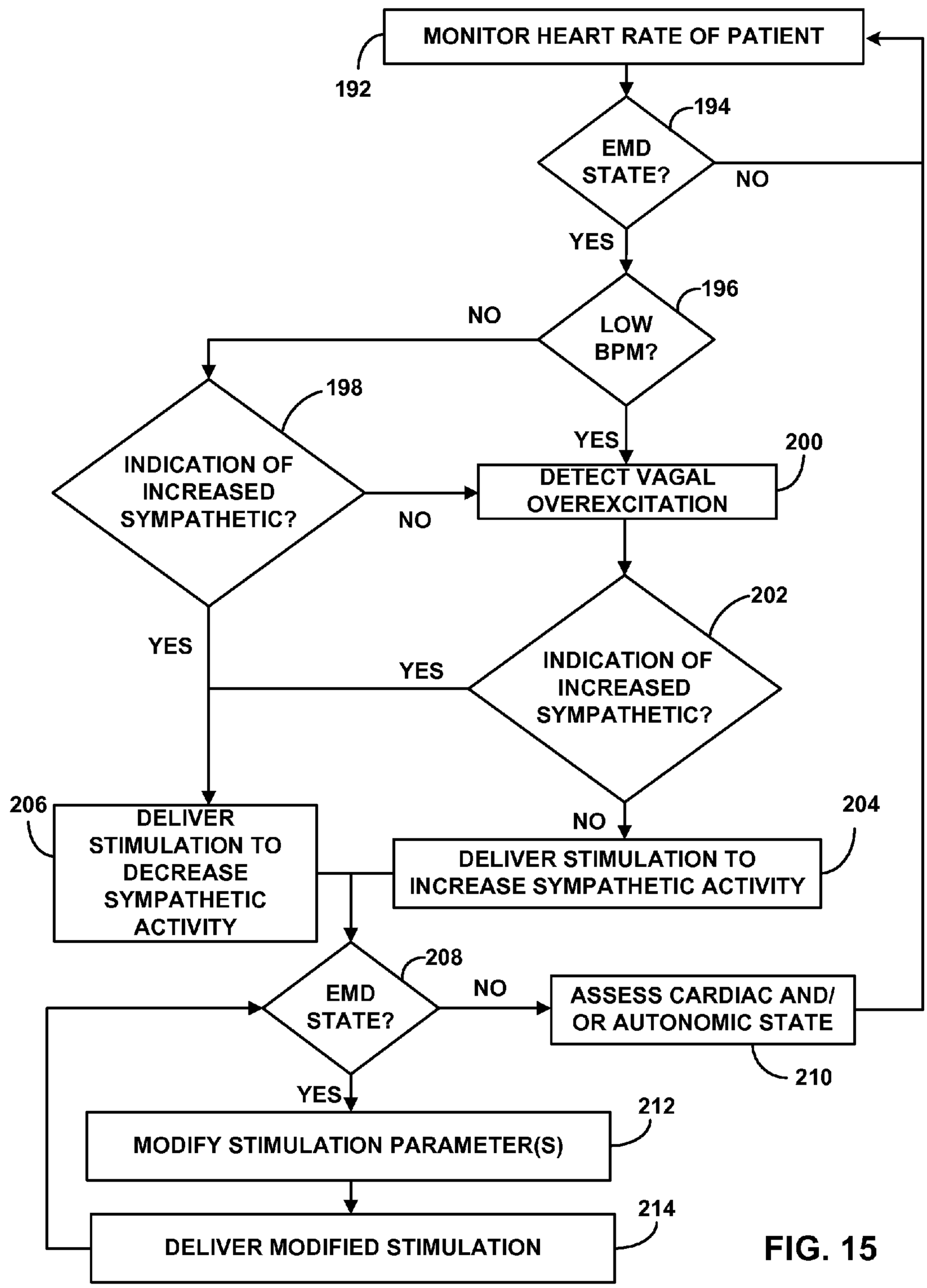
MONITOR HEART RATE OF PATIENT
192
194
EMD STATE?
NO
YES
196
LOW BPM?
NO
198
INDICATION OF INCREASED SYMPATHETIC?
YES
200
DETECT VAGAL OVEREXCITATION
NO
202
INDICATION OF INCREASED SYMPATHETIC?
YES
YES
206
DELIVER STIMULATION TO DECREASE SYMPATHETIC ACTIVITY
NO
204
DELIVER STIMULATION TO INCREASE SYMPATHETIC ACTIVITY
208
EMD STATE?
NO
ASSESS CARDIAC AND/ OR AUTONOMIC STATE
210
YES
212
MODIFY STIMULATION PARAMETER(S)
214
DELIVER MODIFIED STIMULATION

FIG. 15

DETECTING AND TREATING ELECTROMECHANICAL DISSOCIATION OF THE HEART

This application claims the benefit of U.S. Provisional Application No. 61/148,674, entitled, "DETECTING AND TREATING ELECTROMECHANICAL DISSOCIATION OF THE HEART," and filed on Jan. 30, 2009, the entire content of which is incorporated herein by reference.

TECHNICAL FIELD

The disclosure relates to medical devices and, in particular, medical devices configured to deliver electrical stimulation therapy to a patient.

BACKGROUND

A wide variety of implantable medical devices that deliver a therapy or monitor a physiologic condition of a patient have been clinically implanted or proposed for clinical implantation in patients. Some implantable medical devices may employ one or more elongated electrical leads and/or sensors. Such implantable medical devices may deliver therapy or monitor the heart, muscle, nerve, brain, stomach or other organs. In some cases, implantable medical devices deliver electrical stimulation therapy and/or monitor physiological signals via one or more electrodes or sensor elements, which may be included as part of one or more elongated implantable medical leads. Implantable medical leads may be configured to allow electrodes or sensors to be positioned at desired locations for delivery of stimulation or sensing electrical depolarizations. For example, electrodes or sensors may be located at a distal portion of the lead. A proximal portion of the lead may be coupled to an implantable medical device housing, which may contain electronic circuitry such as stimulation generation and/or sensing circuitry.

For example, implantable cardiac devices, such as cardiac pacemakers or implantable cardioverter defibrillators, provide therapeutic stimulation to the heart by delivering electrical signals such as pulses or shocks for pacing, cardioversion or defibrillation pulses via electrodes of one or more implantable leads. In some cases, an implantable cardiac device may sense intrinsic depolarizations of the heart, and control the delivery of therapeutic stimulation to the heart based on the sensing. When an abnormal rhythm of the heart is detected, such as bradycardia, tachycardia or fibrillation, an appropriate electrical therapy (e.g., in the form of pulses) may be delivered to restore the normal rhythm. For example, in some cases, an implantable medical device may deliver pacing, cardioversion or defibrillation therapy to the heart of the patient upon detecting ventricular tachycardia, and deliver cardioversion or defibrillation therapy to a patient's heart upon detecting ventricular fibrillation. Some medical device systems that include a neurostimulator in addition to implantable cardiac device have also been proposed.

SUMMARY

In general, the disclosure is directed to therapy systems for treating the electromechanical dissociation (EMD) of a heart of a patient. In an EMD state, the heart of the patient exhibits what may be considered typical electrical activity (e.g., a normal sinus rhythm observed in an electrogram or electrocardiogram), but does not exhibit proper mechanical contractions. In some examples, a therapy system detects an EMD state of the heart of the patient based on one or more sensed physiological parameters of a patient that indicate whether the heart is sufficiently contracting. The therapy system may be configured to sense such physiological parameters in conjunction with the delivery of cardioversion or defibrillation therapy by a cardiac device. The heart may be susceptible to entering an EMD state after delivery of such cardioversion or defibrillation therapy.

When the therapy system determines that the heart of a patient is in an EMD state, the therapy system generates and delivers electrical stimulation to a tissue site of the patient to modulate afferent nerve activity and/or inhibit efferent nerve activity. Such electrical stimulation may be configured to effectively treat the EMD state, e.g., by promoting mechanical contraction of the heart. The therapy system may deliver the electrical stimulation to one or more tissue sites including least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

In some examples, the therapy system may monitor autonomic nervous system activity of a patient. When the therapy system determines that the heart of a patient is in an EMD state, the therapy system determines autonomic activity (e.g., sympathetic and/or parasympathetic nervous system activity) associated with the EMD state. Electrical stimulation delivered to the patient to treat the EMD state may then be determined based on the autonomic activity associated with the EMD state. For example, the therapy system may determine that a relatively low level of sympathetic nervous system activity is exhibited by the patient during the occurrence of the EMD state. In such an example, the therapy system may deliver electrical stimulation to the patient configured to increase sympathetic nervous system activity in the patient. In this manner, as the autonomic nervous system activity associated with the EMD state may be an underlying cause of the EMD state, the stimulation delivered to the patient may effectively treat the EMD state based on the autonomic nervous system activity associated with the detected EMD state.

In one example, the disclosure is directed to a method comprising sensing at least one physiological parameter of a patient, determining whether a heart of the patient is in an electromechanical dissociation state based on the at least one sensed physiological parameter, and delivering electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electromechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

In another example, the disclosure is directed to a medical system comprising a sensor that senses at least one physiological parameter of a patient, a processor that determines whether a heart of the patient is in an electrical mechanical dissociation state based on the at least one sensed physiological parameter, and a stimulation generator that delivers electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity when the processor determines that the heart is in the electrical mechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

In another example, the disclosure is directed to a medical system comprising means for sensing at least one physiological parameter of a patient, means for determining whether a heart of the patient is in an electrical mechanical dissociation state of a heart of the patient based on the at least one sensed physiological parameter, and means for

delivering electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

In another example, the disclosure is direct to a method of treating an electromechanical disassociation state of a heart of a patient, wherein the method is characterized by implanting a medical device system in a patient, where the medical device system comprises a stimulation generator and a processor that determines whether the heart of the patient is in the electrical mechanical dissociation state based on at least one sensed physiological parameter and controls the stimulation generator to deliver electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

In another example, the disclosure is directed to a method comprising determining whether a heart of a patient is in an electromechanical dissociation state, determining autonomic activity of the patient associated with the electromechanical dissociation state, and delivering electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state.

In another example, the disclosure is directed to a medical system comprising a processor that determines whether a heart of the patient is in an electrical mechanical dissociation state and that determines autonomic activity of the patient associated with the electromechanical dissociation state, and a stimulation generator that delivers electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state.

In another example, the disclosure is directed to a medical system comprising means for determining whether a heart of a patient is in an electromechanical dissociation state, means for determining autonomic activity of the patient associated with the electromechanical dissociation state, and means for delivering electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state.

In another example, the disclosure is directed to a method of treating an electromechanical disassociation state of a heart of a patient, wherein the method is characterized by implanting a medical device system in a patient, where the medical device system comprises a stimulation generator, and a processor that determines whether a heart of a patient is in an electrical mechanical dissociation state, determines autonomic nervous system activity of the patient associated with the electromechanical dissociation state upon determining that the heart is in the electromechanical dissociation state, and controls the stimulation generator to deliver electrical stimulation to the patient based on the determined autonomic nervous system activity of the patient associated with the electromechanical dissociation state.

The details of one or more examples are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the devices, systems, and techniques of the disclosure will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF DRAWINGS

FIG. **1** is a conceptual diagram illustrating an example therapy system that includes an implantable cardiac device (ICD) and an implantable neurostimulator (INS).

FIG. **2** is a conceptual diagram illustrating another example therapy system that includes an ICD and an INS.

FIG. **3** is a conceptual diagram illustrating the ICD and associated leads of the therapy systems of FIGS. **1** and **2** in greater detail.

FIG. **4** is a conceptual diagram illustrating another example ICD lead configuration.

FIG. **5** is a conceptual diagram of another example therapy system that includes two medical devices to provide therapy to a patient.

FIG. **6** is a functional block diagram of an example ICD that generates and delivers cardiac rhythm therapy to a heart of a patient.

FIG. **7** is a functional block diagram of an example INS that generates and delivers electrical stimulation to a target tissue site of a patient.

FIG. **8** is a functional block diagram of an example medical device programmer.

FIG. **9** is a flow diagram illustrating an example technique for determining when a heart of a patient is in an EMD state and delivering electrical stimulation to a patient upon determining the heart is in the EMD state.

FIG. **10** is a flow diagram illustrating an example technique for determining when a heart is in an EMD state.

FIG. **11** is a flow diagram illustrating another example technique for determining when a heart is in an EMD state.

FIG. **12** is a flow diagram illustrating an example technique for monitoring a heart of a patient for an EMD state following delivery of defibrillation therapy to the heart.

FIG. **13** is a flow diagram illustrating another example technique for monitoring a heart of a patient for an EMD state following the delivery of defibrillation therapy to the heart.

FIG. **14** is a flow diagram illustrating an example technique for delivering stimulation to a patient when the heart of the patient is in an EMD state.

FIG. **15** is a flow diagram illustrating an example technique for delivering stimulation to a patient when the heart of the patient is in an EMD state.

DETAILED DESCRIPTION

FIG. **1** is a conceptual diagram illustrating an example therapy system **10** that may be used to provide therapy to patient **12**. Therapy system **10** includes implantable cardiac device (ICD) **16**, which is connected to leads **18**, **20**, and **22**, and programmer **24**. ICD **16** may comprise, for example, an implantable pacemaker, cardioverter, and/or defibrillator that provide therapy to heart **14** of patient **12** via electrodes connected to one or more of leads **18**, **20**, and **22**. In some examples, ICD **16** may deliver pacing pulses, but not cardioversion or defibrillation pulses, while in other examples, ICD **16** may deliver cardioversion or defibrillation pulses, but not pacing pulses. In addition, in further examples, ICD **16** may deliver pacing, cardioversion, and defibrillation pulses.

In some examples, ICD **16** may not deliver cardiac rhythm management therapy to heart **14**, but may instead only sense electrical cardiac signals of heart **14** and/or other physiological parameters of patient **12** (e.g., blood oxygen saturation, blood pressure, temperature, heart rate, respiratory rate, and the like), and store the electrical cardiac

signals and/or other physiological parameters of patient **12** for later analysis by a clinician. In such examples, ICD **16** may be referred to as a patient monitoring device. Examples of patient monitoring devices include, but are not limited to, the Reveal Plus Insertable Loop Recorder, which is available from Medtronic, Inc. of Minneapolis, Minn. For ease of description, ICD **16** will be referred to herein as a cardiac rhythm management therapy delivery device.

Therapy system **10** further comprises implantable electrical stimulator **26**, which is coupled to lead **28** and **31**. Electrical stimulator **26** may also be referred to as an implantable neurostimulator (INS) **26**. INS **26** may be any suitable implantable medical device (IMD) that includes a signal generator that generates electrical stimulation signals that may be delivered to a tissue site of patient **12**, e.g., tissue proximate a vagus nerve, a spinal cord or heart **14** of patient **12**. Although INS **26** is referred to throughout the remainder of the disclosure as a "neurostimulator" and as delivering neurostimulation pulses, in other examples, INS **26** may deliver electrical stimulation to any suitable nonmyocardial tissue site within patient **12**, which may or may not be proximate a nerve.

In some examples, INS **26** may deliver stimulation signals to any suitable tissue site to modulate the activity of the autonomic nervous system of patient **12**, e.g., parasympathetic, sympathetic and/or neurohormonal activity. For example, based on autonomic activity associated with an detected electromechanical disassociation (EMD) state of heart **14**, INS **26** may deliver stimulation signals to any suitable tissue site to increase or decrease sympathetic nervous system activity. In other examples, INS **26** may deliver electrical stimulation signals to any suitable tissue site to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the EMD state.

In some examples, the target tissue site for therapy delivery by INS **26** may include at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site. A nonmyocardial tissue site may include a tissue site that does not include cardiac muscle (e.g., the myocardium). For example, a nonmyocardial tissue site may be proximate a muscle other than cardiac muscle, an organ other than the heart, or neural tissue. A tissue site proximate a nerve may be a neural tissue site to which delivery of electrical stimulation may activate the nerve. In some examples, a tissue site proximate a nerve may be in a range of about zero centimeters to about ten centimeters from the nerve, although other distance ranges are contemplated and may depend upon the nerve. The nonmyocardial tissue site may include extravascular tissue sites or intravascular tissue sites. An extravascular tissue site may be outside of heart **14** and outside of arteries, veins, or other vasculature of patient **12**. In other examples, stimulation may be delivered to a nonmyocardial tissue site via electrodes of an intravascular lead that is implanted within vasculature. A nonvascular cardiac tissue site may include, for example, a cardiac fat pad.

In some examples, INS **26** may deliver electrical stimulation therapy to a nerve of patient **12** via a lead implanted within vasculature (e.g., a blood vessel) of patient **12**. In some examples, INS **26** may deliver electrical stimulation that is delivered to peripheral nerves that innervate heart **14**, or fat pads on heart **14** that may contain nerve bundles. In the example shown in FIG. **1**, electrodes of lead **28** are positioned outside the vasculature of patient **12** and positioned to deliver electrical stimulation to a vagus nerve (not shown) of patient **12**.

In some examples, delivery of electrical stimulation by INS **26** to a nonmyocardial tissue site or nonvascular cardiac tissue site may help modulate an autonomic nervous system of patient **12** and/or provide cardioprotective benefits to patient **12**. For example, delivery of electrical stimulation to a tissue site proximate a nerve of patient **12** may help treat heart failure. In addition, delivery of electrical stimulation to a tissue site proximate a nerve of patient **12** to modulate an autonomic nervous system of patient **12** may help reduce or eliminate cardiovascular conditions such as bradycardia, tachycardia, unhealthy cardiac contractions, ischemia, inefficient heart pumping, inefficient collateral circulation of heart **14** or cardiac muscle trauma. In some examples, delivery of electrical stimulation to a tissue site proximate a nerve of patient **12** to modulate autonomic nervous system activity may help treat heart **14** when in an EMD state. Delivery of electrical stimulation by INS **26** may complement antitachycardia therapy (e.g., antitachycardia pacing, cardioversion or defibrillation) by ICD **16** or provide backup therapy to the cardiac rhythm therapy provided by ICD **16**. For example, if ICD **16** is unavailable to provide therapy to patient **12**, e.g., due to a low power level, INS **26** may deliver therapy to patient **12** to help terminate or prevent a cardiac event (e.g., tachycardia).

As described in further detail below, INS **26** may also deliver therapy to modulate afferent nerve activity and/or inhibit efferent nerve activity of patient **12** in order to treat EMD of heart **14**. In general, EMD, which also may be known as pulseless electrical activity (PEA), refers to a patient condition characterized by the persistence of electrical activity in heart **14** without associated mechanical contraction, with minimal mechanical contraction or substantially ineffective mechanical contraction. EMD may be described as a clinical condition characterized by unresponsiveness and lack of palpable pulse in the presence of organized cardiac electrical activity. In some cases, heart **14** may be prone to enter an EMD state after the delivery of cardioversion or defibrillation therapy, e.g., by ICD **16**, as previously described, although it is not limited to such situations.

When heart **14** is in an EMD state, the electrical activity of heart **14** may be indicative of a heart functioning in a manner that includes mechanical contraction. For example, an electrocardiogram (ECG) or electrogram (EGM) of heart **14** may indicate a sinus rhythm of heart **14**. However, despite the presence of relatively normal electrical activity, heart **14** may not be mechanically contracting in a physiologically significant manner. Physiologically significant mechanical contractions may be, for example, contractions necessary to supply the cardiac output (e.g., sufficient blood flow) to meet the needs of the patient's body. Thus, although heart **14** may produce weak contractions when in an EMD state, the contractions that produce the blood perfusion necessary to sustain life are not present despite the persistence of electrical activity in heart **14**. In some cases, EMD may be associated with the presence of electrical activity and the absence of cardiac contractions.

In some examples, EMD may not be readily detectable by only monitoring the electrical activity of the heart of a patient. Accordingly, in order to detect EMD of heart **14**, therapy system **10** may include one or more sensors that sense physiological parameters that indicate whether heart **14** is contracting in a physiologically significant manner. Examples of physiological parameters that may indicate the extent to which heart **14** is contracting include blood pressure, blood flow, blood oxygen saturation level, movement of cardiac muscles, heart sounds corresponding to contrac-

tion, heart images (e.g., based on implantable ultrasonic techniques), tissue perfusion and the like.

In some examples, INS **26** sense one or more physiological parameters of patient **12** that indicate the relative level of heart contraction. The sensed physiological parameter may be used to determine when heart **14** is in an electromechanical dissociation (EMD) state. If INS **26** determines that heart **14** is in an EMD state, INS **26** may deliver stimulation therapy to patient **12** in order to terminate the EMD state of heart **14**. The stimulation therapy modulates afferent nerve activity and/or inhibits efferent nerve activity of patient **12** in order to terminate the EMD state. The electrical stimulation therapy may be delivered by INS **26** to a tissue site of patient **12**, such as, e.g., nonmyocardial tissue site or a nonvascular cardiac tissue site.

In the example shown in FIG. **1**, INS **26** may sense one or more physiological parameter via one or more sensors of lead **31**, where the sensors are located proximate to heart **14**. In some examples, ICD **16** may additionally, or alternatively, sense one or more physiological parameters of patient **12** that may be used to determine whether heart **14** is in an EMD state. In addition, system **10** may include a sensing device separate than that of ICD **16** and INS **26** that senses one or more physiological parameters used to determine when heart **14** is in an EMD state.

As described in further detail below, in some examples, INS **26** and/or ICD **16** monitors autonomic nervous system activity of patient **12** to determine autonomic nervous system activity associated with an EMD state of heart **14**. The autonomic nervous system associated with a detected EMD state of heart **14** of patient **12** can be the state of the autonomic nervous system at the time the EMD state is detected, at a time preceding the detection of the EMD state (e.g., preceding the EMD state detection by a predetermined period of time), or at a time following the detection of the EMD state. In examples described herein, the autonomic nervous system associated with a detected EMD state of heart **14** of patient **12** includes at least the state of the autonomic nervous system activity at the time ICD **16** or INS **26** detected the EMD state of patient **12**. Autonomic nervous system activity of patient **12** may include sympathetic nervous system activity and/or parasympathetic nervous system activity.

In some examples, the behavior of autonomic nervous system activity may be an underlying cause of the EMD state in patient **12**. In one example, depressed sympathetic nervous system activity may cause heart **14** to enter or maintain an EMD state, while in other examples, overexcited sympathetic nervous system activity may cause heart **14** to enter or maintain an EMD state. As such, upon detecting that heart **14** is in an EMD state, INS **26** and/or ICD **16** may determine the whether the EMD state is accompanied by relatively low or high level of sympathetic or other autonomic nervous system activity. As discussed in further detail with respect to FIGS. **14** and **15**, ICD **16** and/or INS **26** or another device can determine whether sympathetic activity of patient **12** is relatively high or low by comparing one or more physiological parameters to threshold values associated with the relatively low and relatively high sympathetic activity designations.

The autonomic activity associated with a detected EMD state may be used to select the type (e.g., as indicated by stimulation parameter values or target stimulation sites) of electrical stimulation delivered to patient **12** by INS **26** (or ICD **16**) to treat the EMD state. For example, if depressed sympathetic nervous system activity is associated with a detected EMD state, INS **26** may deliver electrical stimulation to patient **12** configured to increase sympathetic nervous system activity. Conversely, if overexcited sympathetic nervous system activity is associated with a detected EMD state, INS **26** may deliver electrical stimulation to patient **12** configured to decrease sympathetic nervous system activity.

INS **26** and/or ICD **16** may monitor and determine autonomic nervous system activity of patient **12** using any suitable technique. In some examples, electrical activity of heart **14** may be sensed by ICD **16** and/or INS **26** (e.g., an electrocardiogram (ECG) or electrogram (EGM)) via one or more electrodes on leads **18**, **20**, **22**, **28**, **29** to identify autonomic activity associated with (e.g., temporally correlated with) a detected EMD state. For example, sensed electrical activity of heart **14** may be analyzed by INS **26**, ICD **16** or other device to determine the heart rate of heart **14**. Sensed electrical activity of heart **14** that reflects a relatively low heart rate, such as, e.g., about 20 to 30 beats per minute (BPM) compared to a "normal" heart rate of about 60 to about 70 BPM, may be indicate depressed sympathetic activity. Similarly, sensed electrical activity of heart **14** that reflects a relatively high heart rate, such as, e.g., about 100 to 120 beats per minute (BPM), may be indicate overexcited sympathetic activity. The low heart rate, high heart rate, and/or normal heart rate may be predetermined and stored by ICD **16**, INS **26** or another device. In other examples, the normal heart may be determined based on, for example, an average sensed heart rate for a predetermined period of time preceding the detection of the EMD state. In this way, the "normal" heart rate may be a dynamically changing value.

Additionally or alternatively, heart rate variability (e.g., P-P interval variability and/or R-R interval variability) may also be analyzed by INS **26**, ICD **16** or other device to monitor autonomic activity to treat the detected EMD state of patient **14**. P-P or R-R interval variability refers to the variability in the P-P or R-R interval, i.e., the duration of time between consecutive or successive P or R waves, respectively. In some examples, sensed electrical activity of heart **14** that reflects an increase in heart rate variability may indicate overexcited parasympathetic nervous system activity. In this way, heart rate variability may be used as an indicator for the nature of the autonomic nervous system activity associated with a detected EMD state.

Additionally or alternatively, ICD **16** and/or INS **26** may determine autonomic nervous system activity associated with a detected EMD state of heart **14** by monitoring electrical activity at one or more nerve sites of patient **12** via one or more electrodes on leads **18**, **20**, **22**, **28**, **29**. For example, INS **26** may monitor electrical activity of one or more sympathetic or parasympathetic ganglion of patient **12** via one or more of leads **28**, **29**. Similarly, ICD **16** or INS **26** may monitor electrical activity of the AV node, which may include a large number of parasympathetic nerve fibers. As such, electrical activity monitored at the AV node may be used as an indicator of excited or depressed parasympathetic nervous system activity. Sensed electrical activity from one or more nerve sites may be analyzed by ICD **16** and/or INS **26** to identify depressed or overexcited autonomic nervous system activity that may be associated with an EMD state of patient **12**.

Based on the autonomic activity determined to be associated with the occurrence of a detected EMD state, INS **26** and/or ICD **16** may deliver electrical stimulation to patient **12** that appropriately modulates autonomic nervous system activity of patient **12**. In this way, ICD **16** and/or INS **26** controls the delivery of stimulation to patient **12** based on the autonomic nervous system activity determined to be

associated with the occurrence of a detected EMD state. In some examples, INS **26** stimulates the central nervous system to modulate parasympathetic and/or sympathetic activity. For example, INS **26** may stimulate spinal cord **44** of the central nervous system, e.g., in the cervical, thoracic, and/or lumbar regions. Additionally or alternatively, INS **26** may deliver peripheral nerve stimulation to patient **12** to module autonomic nervous system activity.

INS **26** may stimulate parasympathetic and/or sympathetic ganglia neural tissue of the central nervous system proximate to spinal cord **44**. Stimulating one or more ganglion may allow INS **26** to deliver lower intensity stimulation, e.g., lower amplitude and/or lower frequency, than stimulating tissue of the peripheral nervous system further away from spinal cord **44**. Additionally, in some cases, ganglia may be more convenient to access than peripheral neural tissue further away from spinal cord **44**. For example, implanting leads **28** and **29** proximate to one or more ganglion may be less invasive than implanting leads **28** and proximate to other peripheral neural tissue further away from spinal cord **44**.

Additionally or alternatively, INS **26** may stimulate the brain of patient **12**, e.g., at one or more centers that regulate autonomic activity, such as the dorsal vagal motonucleus, nucleus ambiguus, nucleus tractus solitarii, hypothalamus, and/or spinal intermediolateral column. In such examples, one or more of leads **28** and **29** may be implanted within the brain of patient **12**. Stimulation sites other than those describe herein are contemplated.

The components of ICD **16** and INS **26** are enclosed in separate housings, such that ICD **16** and INS **26** are physically separate devices. In other examples, the functionality of ICD **16** and INS **26** may be performed by an IMD that includes both a cardiac therapy module that generates and delivers at least one of pacing, cardioversion or defibrillation therapy to patient **12** and an electrical stimulation therapy module that generates and delivers electrical stimulation to a target tissue site within patient **12**, which may be proximate a nerve, a nonvascular cardiac tissue site, an extravascular tissue site that is not proximate a nerve.

Leads **18**, **20**, **22** extend into the heart **14** of patient **12** to sense electrical activity of heart **14** and/or deliver electrical stimulation to heart **14**. In the example shown in FIG. **1**, right ventricular (RV) lead **18** extends through one or more veins (not shown), the superior vena cava (not shown), and right atrium **30**, and into right ventricle **32**. Left ventricular (LV) coronary sinus lead **20** extends through one or more veins, the vena cava, right atrium **30**, and into the coronary sinus **34** to a region adjacent to the free wall of left ventricle **36** of heart **14**. Right atrial (RA) lead **22** extends through one or more veins and the vena cava, and into the right atrium **30** of heart **14**. As described in further detail with reference to FIG. **5**, in other examples, an ICD may deliver stimulation therapy to heart **14** by delivering stimulation to a nonmyocardial tissue site in addition to or instead of delivering stimulation via electrodes of intravascular leads **18**, **20**, **22**.

ICD **16** may sense electrical signals attendant to the depolarization and repolarization of heart **14** via electrodes (not shown in FIG. **1**) coupled to at least one of the leads **18**, **20**, **22**. In some examples, ICD **16** provides pacing pulses to heart **14** based on the electrical signals sensed within heart **14**. These electrical signals sensed within heart **14** may also be referred to as cardiac signals or electrical cardiac signals. The configurations of electrodes used by ICD **16** for sensing and pacing may be unipolar or bipolar. ICD **16** may also provide defibrillation therapy and/or cardioversion therapy via electrodes located on at least one of the leads **18**, **20**, **22**. ICD **16** may detect arrhythmia of heart **14**, such as fibrillation of ventricles **32** and **36**, and deliver defibrillation therapy to heart **14** in the form of electrical pulses. In some examples, ICD **16** may be programmed to deliver a progression of therapies, e.g., pulses with increasing energy levels, until a fibrillation of heart **14** is stopped. ICD **16** detects fibrillation employing one or more fibrillation detection techniques known in the art.

In the example of FIG. **1**, INS **26** has been implanted in patient **12** proximate to an nonmyocardial target stimulation site **40**, such as a tissue site proximate a vagus nerve. For example, INS **26** may be subcutaneously or submuscularly implanted in the body of a patient **12** (e.g., in a chest cavity, lower back, lower abdomen, or buttocks of patient **12**). INS **26** provides a programmable stimulation signal (e.g., in the form of electrical pulses or a continuous signal) that is delivered to target stimulation site **40** by implantable medical lead **28**, and more particularly, via one or more stimulation electrodes carried by lead **28**. Proximal end **28**A of lead **28** may be both electrically and mechanically coupled to connector **42** of INS **26** either directly or indirectly (e.g., via a lead extension). In particular, conductors disposed in the lead body may electrically connect stimulation electrodes (and sense electrodes, if present) of lead **28** to INS **26**. Connector **42** may also be referred to as a connector block or a header of INS **26**. Proximal end **31**A of lead **31** may be both electrically and mechanically coupled to connector **42** of INS **26** either directly or indirectly (e.g., via a lead extension). When electrically coupled to INS **26**, sensed information may be communicated from the sensor of lead **31** to INS **26**.

INS **26** may also be referred to as a signal generator. In some examples, lead **28** may also carry one or more sense electrodes to permit INS **26** to sense electrical signals from target stimulation site **40**. Furthermore, in some examples, INS **26** may be coupled to two or more leads, e.g., for bilateral or multi-lateral stimulation.

In other examples, electrodes of lead **28** may be positioned to deliver electrical stimulation to any other suitable nerve, which may be selected to be a nerve that may be modulated to change afferent nerve activity and/or inhibit efferent nerve activity of patient **12** in order to increase the contractility of heart **14**. In addition, in other examples, electrodes of lead **28** or another lead electrically connected to INS **26** may be positioned to deliver stimulation to an organ, muscle or muscle group in patient **12**, which may be selected based on, for example, a therapy regimen selected for a particular patient. For example, INS **26** may also deliver electrical stimulation to a target tissue site **40** that is not proximate to a nerve. For example, in some examples, INS **26** may deliver electrical stimulation to a peripheral nerve field site, whereby electrodes **124** (FIG. **7**) of lead **28** are implanted in a region where patient **12** experiences pain. The pain may be related to stimulation delivered by ICD **16** or a patient condition, such as angina or chronic back pain. As other examples, INS **26** may deliver electrical stimulation to a muscle, muscle group, organ, or other sites that may not be proximate a nerve. Thus, while "neurostimulation" signals are primarily referred to herein, the disclosure is also applicable to examples in which INS **26** delivers electrical stimulation to other tissue sites.

As shown in FIG. **2**, INS **26** may deliver electrical stimulation to spinal cord **44** of patient **12** in order to help modulate an afferent nerve of patient **12**, inhibit efferent nerve activity of patient **12**, or modulate autonomic nervous system activity to improve contractility of heart **14**. In addition, stimulation of spinal cord **44** or nerves branching

therefrom by INS **26** may help prevent or mitigate occurrences of tachyarrhythmias and may facilitate reduction of the level of aggressiveness of the cardiac therapy, such as pacing, cardioversion or defibrillation therapy, delivered by ICD **16**. In this way, ICD **16** and INS **26** may operate in conjunction with each other to help prevent arrhythmias of heart **14** of patient **12**, as well as to terminate detected arrhythmias. In some examples, INS **26** may deliver electrical stimulation during the cardiac refractory period or blanking period to avoid interfering with the cardiac sensing function of ICD **16**.

In some examples, depending upon the neurostimulation target, the delivery of electrical stimulation by INS **26** may also mitigate perceptible discomfort generated from the delivery of pacing pulses or cardioversion/defibrillation shocks by ICD **16**. For example, if INS **26** delivers electrical stimulation to spinal cord **44** of patient **12**, the neurostimulation may produce paresthesia, which may help reduce the discomfort felt by patient **12** from the delivery of stimulation by ICD **16**.

In the example shown in FIG. **2**, INS **26** is coupled to two leads **28**, **29** which may facilitate bilateral spinal cord stimulation of patient **12**. Leads **28**, **29** may be introduced into spinal cord **44** in the thoracic region, as shown in FIG. **2**. In other examples, leads **28**, **29** may be introduced into spinal cord **44** in the cervical or lumbar region. Electrodes of leads **28**, **29** may be positioned within an intrathecal space or epidural space of spinal cord **44**, or, in some examples, adjacent nerves that branch off of spinal cord **44**. In some examples, leads **28**, **29** are implanted within patient **12** and positioned such that electrodes of leads **28**, **29** deliver electrical stimulation to locations proximate to the T1 to T6 thoracic vertebrae of the patient's vertebral column. For example, electrodes of at least one of the leads **28**, **29** may span the T3 to T6 thoracic vertebrae or deliver electrical stimulation to a tissue site proximate at least one of the T3 to T6 thoracic vertebrae. In other examples, leads **28**, **29** may be implanted to deliver electrical stimulation to other regions proximate or within spinal cord **44**, such as over or near other vertebrae.

In some examples, INS **26** delivers therapy to patient **12** with a voltage amplitude of about 0.2 volts to about 12 volts, a pulse duration of about 40 microseconds (μs) to about 600 μs, such as about 50 μs to about 500 μs), and a pulse rate of approximately 1 Hertz (Hz) to approximately 1 kilohertz (e.g., 10 Hz to 100 Hz). However, other stimulation parameter values for INS **26** are contemplated. INS **26** may deliver electrical stimulation to patient **12** substantially continuously or periodically. In some examples, INS **26** may deliver electrical stimulation to patient **12** based on the timing of electrical stimulation by ICD **16**, such as prior to the delivery of electrical stimulation (e.g., antitachycardia pacing or a defibrillation or cardioversion pulse) by ICD **16**, during the delivery of electrical stimulation by ICD **16**, subsequent to the delivery of electrical stimulation by ICD **16** or any combination of the aforementioned times.

In addition, in some examples, INS **26** may deliver electrical stimulation to patient **12** based on a sensed event or, such as atrial or ventricular depolarization, or based on a sensed physiological condition that indicates that heart **14** is in an EMD state. The event or physiological condition may be sensed by ICD **16**, INS **26** or another sensing device. In some examples, the electrical stimulation used to treat the EMD state of heart **14** is configured to modulate afferent nerve activity and/or inhibit efferent nerve activity. In some examples, the electrical stimulation used to treat the EMD state of heart **14** is configured to modulate autonomic nervous system activity, where the type of modulation (e.g., in increase or decrease sympathetic activity) is based on the autonomic nerve activity determined to be associated with the EMD state.

ICD **16** and INS **26** may communicate with each other in order for INS **26** to time the delivery of electrical stimulation based on the delivery of stimulation pulses by ICD **16**, where the stimulation pulses may be pacing pulses or cardioversion/defibrillation pulses. ICD **16** and INS **26** may communicate directly or indirectly (e.g., via an intermediate device, such as programmer **24**) using any suitable communication technique. Examples communication techniques that may be implemented to facilitate communication between ICD **16** and INS **26** may include, for example, electrical signals transmitted through the patient's tissue, radiofrequency (RF) communication techniques, optical communication techniques, ultrasonic communication techniques, and the like. Communication between ICD **16** and INS **26** may be periodic, e.g., according to a regular schedule, or on an as-needed basis, e.g., when ICD **16** delivers cardiac rhythm management therapy to patient **12**.

In other examples, INS **26** may deliver electrical stimulation to patient **12** independently of the cardiac rhythm therapy delivered by ICD **16**. For example, INS **26** may be programmed to deliver electrical stimulation to patient **12** when EMD is detected based on one or more sensed physiological parameters of patient **12**.

The values for the therapy parameters that define the electrical stimulation delivered by INS **26** may be organized into a group of parameter values referred to as a "therapy program" or "therapy parameter set." "Therapy program" and "therapy parameter set" are used interchangeably herein. In the case of electrical stimulation, the therapy parameters may include an electrode combination, an amplitude, which may be a current or voltage amplitude, and a frequency, and, if INS **26** delivers electrical pulses, a pulse width, and a pulse rate for stimulation signals to be delivered to the patient. An electrode combination may include a selected subset of one or more electrodes of lead **28**, as well as lead **29** if INS **26** is connected to two leads **28**, **29**. The electrode combination may also refer to the polarities of the electrodes in the selected subset. By selecting particular electrode combinations, a clinician may target particular anatomic structures within patient **12**. In addition, by selecting values for amplitude, pulse width, and pulse rate, the physician can attempt to generate an efficacious therapy for patient **12** that is delivered via the selected electrode subset. In some cases, INS **26** may deliver stimulation to patient **12** according to a program group that includes more than one therapy program. The stimulation signals according to the different therapy programs in a therapy group may be delivered on a time-interleaved basis or substantially simultaneously.

The electrical stimulation parameters may also include a duty cycle of stimulation signals, a timing of the delivery of the electrical stimulation relative to a cardiac cycle of heart **14** of patient **12**, and a waveform shape or a signal envelope of the electrical stimulation signal. A signal envelope may generally traces the outline of the amplitude of a stimulation signal for a given period of time. The signal envelope may characterize the amplitude ramp-up and ramp-down times, which may be gradual or abrupt.

If INS **26** delivers therapy to patient **12** according to two or more electrode combinations, e.g., according to a therapy program group including two or more therapy programs defining at least two different electrode combinations, time-interleaving the stimulation signals defined each of the

therapy programs may result in stimulation that is sequentially applied to different electrodes.

In some examples, the therapy parameter values with which INS **26** generates electrical stimulation therapy for patient **12** may be selected based on an effect the stimulation has on heart **14**. For example, INS **26** may deliver stimulation to a tissue site within patient **12** according to a first therapy program defining values for a set of therapy parameters, and ICD **16** or INS **26** may assess the response of heart **14** or other portions of the cardiovascular system to the delivery of stimulation by INS **26**. For example, after therapy delivery by INS **26** according to a first therapy program, INS **26** may sense one or more physiological parameters of patient **12** to determine whether heart **14** is mechanically contracting in a physiologically significant manner. Example physiological parameters that indicate heart **14** is mechanically contracting in a physiologically significant manner include, for example, blood pressure, blood flow, tissue perfusion, blood oxygen saturation level, movement of cardiac muscles, heart sounds, heart images, and tissue perfusion. The therapy program may be analyzed based on a positive or negative response of the mechanical activity of heart **14** to the delivery of stimulation by INS **26**. The therapy program may be selected for storage in INS **26**, e.g., for chronic therapy delivery if the test stimulation via the therapy program evoked a positive response by heart **14** and/or other portions of the patient's cardiovascular system.

Programmer **24** of FIGS. **1** and **2** may be a handheld computing device or a computer workstation. Programmer **24** may include a user interface that receives input from a user. The user interface may include, for example, a keypad and a display, which may for example, be a cathode ray tube (CRT) display, a liquid crystal display (LCD) or light emitting diode (LED) display. The keypad may take the form of an alphanumeric keypad or a reduced set of keys associated with particular functions. Programmer **24** can additionally or alternatively include a peripheral pointing device, such as a mouse, via which a user may interact with the user interface. In some examples, a display of programmer **24** may include a touch screen display, and a user may interact with programmer **24** via the display.

A user, such as a physician, technician, or other clinician, may interact with programmer **24** to communicate with ICD **16** and/or INS **26**. For example, the user may interact with programmer **24** to retrieve physiological or diagnostic information from ICD **16** and/or INS **26**. A user may also interact with programmer **24** to program ICD **16** and INS **26**, e.g., select values for operational parameters of ICD **16** and INS **26**, respectively.

For example, the user may use programmer **24** to retrieve information from ICD **16** regarding the rhythm of heart **14**, trends therein over time, or tachyarrhythmia episodes. As another example, the user may use programmer **24** to retrieve information from ICD **16** regarding other sensed physiological parameters of patient **12**, such as electrical depolarization/repolarization signals from the heart (e.g., EGM or ECG signals), intracardiac or intravascular pressure, activity, posture, respiration, heart sounds, or thoracic impedance. As another example, the user may use programmer **24** to retrieve information from ICD **16** regarding the performance or integrity of ICD **16** or other components of system **10**, such as leads **18**, **20**, and **22**, or a power source of ICD **16**.

The user may use programmer **24** to program a therapy progression, select electrodes used to deliver defibrillation pulses, select waveforms for the defibrillation pulse, or select or configure a fibrillation detection algorithm for ICD **16**. The user may also use programmer **24** to program aspects of other therapies provided by ICD **16**, such as cardioversion or pacing therapies. In some examples, the user may activate certain features of ICD **16** by entering a single command via programmer **24**, such as depression of a single key or combination of keys of a keypad or a single point-and-select action with a pointing device.

The user may use programmer **24** to retrieve information from INS **26** regarding the performance or integrity of INS **26** or leads **28**, **29**, **30** (if INS **26** is connected to more than one lead) or a power source of INS **26**. With the aid of programmer **24** or another computing device, a user may select values for therapy parameters for controlling therapy delivery by INS **26**. The values for the therapy parameters may be organized into a group of parameter values referred to as a "therapy program" or "therapy parameter set." "Therapy program" and "therapy parameter set" are used interchangeably herein.

Programmer **24** may communicate with ICD **16** and INS **26** via wireless communication using any techniques known in the art. Examples of communication techniques may include, for example, low frequency or RF telemetry, but other techniques are also contemplated. In some examples, programmer **24** may include a programming head that may be placed proximate to the patient's body near the ICD **16** and INS **26** implant sites in order to improve the quality or security of communication between ICD **16** or INS **26**, respectively, and programmer **24**.

FIG. **3** is a conceptual diagram illustrating ICD **16** and leads **18**, **20**, **22** of therapy system **10** in greater detail. Leads **18**, **20**, **22** may be electrically coupled to a stimulation generator, a sensing module, or other modules ICD **16** via connector block **48**. In some examples, proximal ends of leads **18**, **20**, **22** may include electrical contacts that electrically couple to respective electrical contacts within connector block **48**. In addition, in some examples, leads **18**, **20**, **22** may be mechanically coupled to connector block **48** with the aid of set screws, connection pins or another suitable mechanical coupling mechanism.

Each of the leads **18**, **20**, **22** includes an elongated insulative lead body, which may carry a number of concentric coiled conductors separated from one another by tubular insulative sheaths. In the illustrated example, bipolar electrodes **50** and **52** are located proximate to a distal end of lead **18**. In addition, bipolar electrodes **54** and **56** are located proximate to a distal end of lead **20** and bipolar electrodes **58** and **60** are located proximate to a distal end of lead **22**.

Electrodes **50**, **54** and **58** may take the form of ring electrodes, and electrodes **52**, **56** and **60** may take the form of extendable helix tip electrodes mounted retractably within insulative electrode heads **62**, **64**, and **66**, respectively. Each of the electrodes **50**, **52**, **54**, **56**, **58**, and **60** may be electrically coupled to a respective one of the conductors within the lead body of its associated lead **18**, **20**, **22**, and thereby coupled to respective ones of the electrical contacts on the proximal end of leads **18**, **20** and **22**.

Electrodes **50**, **52**, **54**, **56**, **58**, and **60** may sense electrical signals attendant to the depolarization and repolarization of heart **14**. The electrical signals are conducted to ICD **16** via the respective leads **18**, **20**, **22**. In some examples, ICD **16** also delivers pacing pulses via electrodes **50**, **52**, **54**, **56**, **58**, and **60** to cause depolarization of cardiac tissue of heart **14**. In some examples, as illustrated in FIG. **3**, ICD **16** includes one or more housing electrodes, such as housing electrode **68**, which may be formed integrally with an outer surface of hermetically-sealed housing **70** of ICD **16** or otherwise coupled to housing **70**. In some examples, housing electrode

68 is defined by an uninsulated portion of an outward facing portion of housing 70 of ICD 16. Divisions between insulated and uninsulated portions of housing 70 may be employed to define two or more housing electrodes. In some examples, housing electrode 68 comprises substantially all of housing 70. Any of the electrodes 50, 52, 54, 56, 58, and 60 may be used for unipolar sensing or pacing in combination with housing electrode 68. As described in further detail with reference to FIG. 6, housing 70 may enclose a stimulation generator that generates cardiac pacing pulses and defibrillation or cardioversion shocks, as well as a sensing module for monitoring the patient's heart rhythm. In some examples, housing electrode 68 may be used to deliver neurostimulation signals to a nerve site of patient 12.

Leads 18, 20, 22 also include elongated electrodes 72, 74, 76, respectively, which may take the form of a coil. ICD 16 may deliver defibrillation pulses to heart 14 via any combination of elongated electrodes 72, 74, 76, and housing electrode 68. Electrodes 68, 72, 74, 76 may also be used to deliver cardioversion pulses to heart 14. Electrodes 72, 74, 76 may be fabricated from any suitable electrically conductive material, such as, but not limited to, platinum, platinum alloy or other materials known to be usable in implantable defibrillation electrodes.

The configurations of therapy system 10 illustrated in FIGS. 1-3 are merely examples. In other examples, a therapy system may include epicardial leads and/or patch electrodes instead of or in addition to the transvenous leads 18, 20, 22 illustrated in FIG. 1. Further, ICD 16 and INS 26 need not be implanted within patient 12. In examples in which ICD 16 is not implanted in patient 12, ICD 16 may deliver defibrillation pulses and other therapies to heart 14 via percutaneous leads that extend through the skin of patient 12 to a variety of positions within or outside of heart 14 or via external patch electrodes. In examples in which INS 26 is not implanted in patient 12, INS 26 may deliver electrical stimulation to target tissue sites within patient 12 via external electrodes or via percutaneous leads that extend through the skin of patient 12.

In other examples of therapy systems that provide electrical stimulation therapy to heart 14, a therapy system may include any suitable number of leads coupled to ICD 16, and each of the leads may extend to any location within or proximate to heart 14. Other examples of therapy systems may include three transvenous leads located as illustrated in FIGS. 1 and 3, and an additional lead located within or proximate to left atrium 38. Other examples of therapy systems may include a single lead that extends from ICD 16 into a chamber of heart 14, such as right atrium 30, right ventricle 32 or left ventricle 36, or two leads that extend into a respective one of the right ventricle 26 and right atrium 28. An example of this type of therapy system is shown in FIG. 4.

FIG. 4 is a conceptual diagram illustrating another example of therapy system 78, which includes ICD 16 connected to two leads 18, 22, rather than three leads as shown in FIGS. 1-3. Leads 18, 22 are implanted within right ventricle 32 and right atrium 30, respectively. Therapy system 78 shown in FIG. 4 may be useful for providing defibrillation and pacing pulses to heart 14. Therapy system 78 may further include INS 26 (not shown in FIG. 4), which is configured to deliver electrical stimulation therapy to modulate an autonomic nervous system of patient 12, (e.g., via stimulation of a vagus nerve or within spinal cord 44) in order to help prevent or mitigate an arrhythmia of patient 12 or to help improve the quality of mechanical contractions of heart 14 when in an EMD state.

FIG. 5 is a conceptual diagram of another example therapy system 80 that includes two medical devices to provide therapy to patient 12. In addition to INS 26 (lead 31 is not shown in FIG. 5), therapy system 80 includes ICD 82, which delivers electrical stimulation to heart 14 without intravascular leads. ICD 82 is coupled to extravascular leads 83, 84, which each include at least one electrode 85, 86, respectively. Electrodes 85, 86 may be subcutaneous coil electrodes, which may be positioned within a subcutaneous tissue layer of patient 12. In other examples, electrodes 85, 86 may comprise any other suitable type of extravascular electrode. For example, electrodes 85, 86 may include any other type of subcutaneous electrode, such as subcutaneous ring electrodes, subcutaneous plate electrodes, subcutaneous patch or pad electrodes, or any other type of electrode, such as a submuscular electrode, an epicardial electrode or an intramural electrode.

Electrodes 85 may be located within the thoracic cavity of patient 12 proximate to right ventricle 32 (FIG. 1), on the patient's side or back, or any other portion of the body appropriate for providing electrical stimulation to heart 14. Electrode 86 may be located within the thoracic cavity of patient 12 proximate left ventricle 36 (FIG. 1), on the patient's side or back, or any other portion of the body appropriate for providing electrical stimulation to the heart. Similar extravascular electrodes are disclosed in commonly-assigned U.S. Pat. No. 5,261,400 to Bardy, which is entitled "DEFIBRILLATOR EMPLOYING TRANSVENOUS AND SUBCUTANEOUS ELECTRODES AND METHOD OF USE" and issued Nov. 16, 1993, and U.S. Pat. No. 5,292,338 to Bardy, which is entitled "ATRIAL DEFIBRILLATOR EMPLOYING TRANSVENOUS AND SUBCUTANEOUS ELECTRODES AND METHOD OF USE" and issued Mar. 8, 1994. U.S. Pat. Nos. 5,261,400 and 5,292,338 are incorporated herein by reference in their entireties.

Leads 83, 84 may be electrically coupled to stimulation modules, and, in some cases, sensing modules, that are enclosed within outer housing 87 of ICD 82. As with housing 70 of ICD 16 (FIG. 3), outer housing 87 may comprise a hermetic housing that substantially encloses the components of ICD 82, such as a sensing module, stimulation generator, processor and the like. Components of an example ICD 16 or ICD 82 are described with respect to FIG. 6. ICD 82 may deliver electrical stimulation (e.g., pacing, cardioversion or defibrillation pulses) to heart 14 between electrodes 85, 86 e.g., in a bipolar configuration. In other examples, ICD 82 may deliver electrical stimulation to heart 14 between electrodes 85 and housing 87 (or an electrode attached to an outer surface of housing 87), or between electrode 86 and housing 87, e.g., in a unipolar configuration.

While the disclosure primarily refers to therapy system 10 including ICD 16 (FIG. 1) and INS 26, the description of the techniques, systems, and devices herein are also applicable to therapy system 80 including ICD 82 and INS 26.

FIG. 6 is a functional block diagram of an example configuration of ICD 16, which includes processor 90, memory 92, stimulation generator 94, sensing module 96, telemetry module 98, and power source 100. The block diagram shown in FIG. 6 may also illustrate an example configuration of ICD 82 (FIG. 5). Memory 92 includes computer-readable instructions that, when executed by processor 90, cause ICD 16 and processor 90 to perform various functions attributed to ICD 16 and processor 90 herein. Memory 92 may include any volatile, non-volatile, magnetic, optical, or electrical media, such as a random access memory (RAM), read-only memory (ROM), non-volatile

RAM (NVRAM), electrically-erasable programmable ROM (EEPROM), flash memory, or any other digital media.

Processor **90** may include any one or more of a microprocessor, a controller, a digital signal processor (DSP), an application specific integrated circuit (ASIC), a field-programmable gate array (FPGA), or equivalent discrete or integrated logic circuitry. In some examples, processor **90** may include multiple components, such as any combination of one or more microprocessors, one or more controllers, one or more DSPs, one or more ASICs, or one or more FPGAs, as well as other discrete or integrated logic circuitry. The functions attributed to processor **90** herein may be embodied as software, firmware, hardware or any combination thereof. Processor **90** controls stimulation generator **94** to deliver stimulation therapy to heart **14** according to a selected one or more of therapy programs, which may be stored in memory **92**. Specifically, processor **90** may control stimulation generator **94** to deliver electrical pulses with the amplitudes, pulse widths, frequency, or electrode polarities specified by the selected one or more therapy programs.

Stimulation generator **94** is electrically coupled to electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76**, e.g., via conductors of the respective lead **18**, **20**, **22**, or, in the case of housing electrode **68**, via an electrical conductor disposed within housing **70** of ICD **16**. Stimulation generator **94** is configured to generate and deliver electrical stimulation therapy to heart **14** to manage rhythm of heart **14**. For example, stimulation generator **94** may deliver defibrillation shocks to heart **14** via at least two electrodes **68**, **72**, **74**, **76**. Stimulation generator **94** may deliver pacing pulses via ring electrodes **50**, **54**, **58** coupled to leads **18**, **20**, and **22**, respectively, helical electrodes **52**, **56**, and **60** of leads **18**, **20**, and **22**, respectively, and/or housing electrode **68**. In some examples, stimulation generator **94** delivers pacing, cardioversion or defibrillation therapy in the form of electrical pulses. In other examples, stimulation generator **94** may deliver one or more of these types of therapy in the form of other signals, such as sine waves, square waves, or other substantially continuous time signals.

In some examples, stimulation generator **94** may include a switch module and processor **90** may use the switch module to select, e.g., via a data/address bus, which of the available electrodes are used to deliver defibrillation pulses or pacing pulses. The switch module may include a switch array, switch matrix, multiplexer, or any other type of switching device suitable to selectively couple stimulation energy to selected electrodes. In other examples, however, stimulation generator **94** may independently deliver stimulation to electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76** or selectively sense via one or more of electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76** without a switch matrix.

Sensing module **96** monitors signals from at least one of electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76** in order to monitor electrical activity of heart **14**, e.g., via an EGM signal. Sensing module **96** may also include a switch module (not shown in FIG. **6**) to select which of the available electrodes are used to sense the heart activity. In some examples, processor **90** may select the electrodes that function as sense electrodes via the switch module within sensing module **96**, e.g., by providing signals via a data/address bus. In some examples, sensing module **96** includes one or more sensing channels, each of which may comprise an amplifier. In response to the signals from processor **90**, the switch module of within sensing module **96** may couple the outputs from the selected electrodes to one of the sensing channels.

In some examples, sensing module **96** may include a plurality of channels. One channel of sensing module **96** may include an R-wave amplifier that receives signals from electrodes **50** and **52**, which are used for pacing and sensing in right ventricle **32** of heart **14**. Another channel may include another R-wave amplifier that receives signals from electrodes **54** and **56**, which are used for pacing and sensing proximate to left ventricle **36** of heart **14**. In some examples, in one operating mode of sensing module **96**, the R-wave amplifiers may take the form of an automatic gain controlled amplifier that provides an adjustable sensing threshold as a function of the measured R-wave amplitude of the heart rhythm.

In addition, in some examples, one channel of sensing module **96** may include a P-wave amplifier that receives signals from electrodes **58** and **60**, which are used for pacing and sensing in right atrium **30** of heart **14**. In some examples, in one operating mode of sensing module **96**, the P-wave amplifier may take the form of an automatic gain controlled amplifier that provides an adjustable sensing threshold as a function of the measured P-wave amplitude of the heart rhythm. Examples of R-wave and P-wave amplifiers are described in U.S. Pat. No. 5,117,824 to Keimel et al., which issued on Jun. 2, 1992 and is entitled, "APPARATUS FOR MONITORING ELECTRICAL PHYSIOLOGIC SIGNALS," and is incorporated herein by reference in its entirety. Other amplifiers may also be used. Furthermore, in some examples, one or more of the sensing channels of sensing module **96** may be selectively coupled to housing electrode **68**, or elongated electrodes **72**, **74**, or **76**, with or instead of one or more of electrodes **50**, **52**, **54**, **56**, **58** or **60**, e.g., for unipolar sensing of R-waves or P-waves in any of chambers **30**, **32**, or **36** of heart **14**.

In some examples, sensing module **96** includes a channel that comprises an amplifier with a relatively wider pass band than the R-wave or P-wave amplifiers. Signals from the selected sensing electrodes that are selected for coupling to this wide-band amplifier may be provided to a multiplexer, and thereafter converted to multi-bit digital signals by an analog-to-digital converter for storage in memory **92** as an electrogram (EGM). In some examples, the storage of such EGMs in memory **92** may be under the control of a direct memory access circuit. Processor **90** may employ digital signal analysis techniques to characterize the digitized signals stored in memory **92** to detect and classify the patient's heart rhythm from the electrical signals. Processor **90** may detect and classify the heart rhythm of patient **12** by employing any of the numerous signal processing methodologies known in the art.

In some examples, sensing module **96** may monitor electrical activity of heart **14** via at least one of electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76**. The sensed electrical activity may be analyzed by processor **90** to determine if the electrical activity is consistent with that of heart **14** generating mechanical contractions. As described in further detail below, the sensed electrical activity may be evaluated in view of the one or more physiological parameters of patient **12** other than electrical cardiac activity to determine an EMD state of heart **14**. For example, if the sensed electrical cardiac activity indicates heart **14** is in a sinus rhythm but the one or more sensed physiological parameters of patient **12** indicate heart **14** is not generating mechanical contractions or physiologically significant mechanical contractions, then either ICD **16**, INS **26** or another device (e.g., programmer **24**) may determine that heart **14** is in an EMD state. Upon determining heart **14** is in an EMD state, electrical stimulation therapy may be

delivered to a tissue site of patient **12** to modulate afferent nerve activity and/or inhibit efferent activity. Such stimulation may help terminate the EMD state by, for example, increasing the contraction of cardiac muscle of heart **14**. In other examples, INS **26** or a suitable sensing device, rather than ICD **16**, may sense the electrical activity of heart **14**, as described, to determine if heart **14** is in an EMD state.

Additionally or alternatively, the electrical activity of heart **14** monitored by sensing module **96** may be analyzed by processor **90** to determine autonomic nervous system activity associated with an EMD state of heart **14**. If the sensed electrical activity reflects depressed or overexcited autonomic activity (e.g., sympathetic or parasympathetic nervous system activity) associated with an EMD state, then INS **26**, ICD **16**, or other device may deliver electrical stimulation to module autonomic activity of patient **12** based on the autonomic activity determined to be associated with the EMD state. For example, if processor **90** or a processor of INS **26** determines that the sensed electrical activity indicates overexcited sympathetic activity (e.g., based on a relatively high heart rate) just before or during the detection of an EMD state, then INS **26** can control the delivery of electrical stimulation therapy to a nonmyocardial tissue site or a nonvascular cardiac tissue site of patient **12** to decrease or depress sympathetic activity. Such stimulation may help terminate the EMD state and help address an underlying cause of the EMD state. In other examples, INS **26** or a suitable sensing device, rather than ICD **16**, may sense the electrical activity of heart **14**, as described, to determine autonomic nervous system activity associated with an EMD state.

If ICD **16** is configured to generate and deliver pacing pulses to heart **14**, processor **90** may include a pacer timing and control module, which may be embodied as hardware, firmware, software, or any combination thereof. The pacer timing and control module may comprise a dedicated hardware circuit, such as an ASIC, separate from other processor **90** components, such as a microprocessor, or a software module executed by a component of processor **90**, which may be a microprocessor or ASIC. The pacer timing and control module may include programmable counters which control the basic time intervals associated with DDD, VVI, DVI, VDD, AAI, DDI, DDDR, VVIR, DVIR, VDDR, AAIR, DDIR and other modes of single and dual chamber pacing. In the aforementioned pacing modes, "D" may indicate dual chamber, "V" may indicate a ventricle, "I" may indicate inhibited pacing (e.g., no pacing), and "A" may indicate an atrium. The first letter in the pacing mode may indicate the chamber that is paced, the second letter may indicate the chamber in which an electrical signal is sensed, and the third letter may indicate the chamber in which the response to sensing is provided. When a pacing code includes "D" as the third letter in the code, it may indicate that the sensed signal is used for tracking purposes.

Intervals defined by the pacer timing and control module within processor **90** may include atrial and ventricular pacing escape intervals, refractory periods during which sensed P-waves and R-waves are ineffective to restart timing of the escape intervals, and the pulse widths of the pacing pulses. As another example, the pacer timing and control module may define a blanking period, and provide signals from sensing module **96** to blank one or more channels, e.g., amplifiers, for a period during and after delivery of electrical stimulation to heart **14**. The durations of these intervals may be determined by processor **90** in response to stored data in memory **92**. The pacer timing and control module of processor **90** may also determine the amplitude of the cardiac pacing pulses.

During pacing, escape interval counters within the pacer timing/control module of processor **90** may be reset upon sensing of R-waves and P-waves. Stimulation generator **94** may include pacer output circuits that are coupled, e.g., selectively by a switching module, to any combination of electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76** appropriate for delivery of a bipolar or unipolar pacing pulse to one of the chambers of heart **14**. Processor **90** may reset the escape interval counters upon the generation of pacing pulses by stimulation generator **94**, and thereby control the basic timing of cardiac pacing functions, including anti-tachyarrhythmia pacing.

The value of the count present in the escape interval counters when reset by sensed R-waves and P-waves may be used by processor **90** to measure the durations of R-R intervals, P-P intervals, P-R intervals and R-P intervals, which are measurements that may be stored in memory **92**. Processor **90** may use the count in the interval counters to detect a tachyarrhythmia event, such as ventricular fibrillation event or ventricular tachycardia event. Upon detecting a threshold number of tachyarrhythmia events, processor **90** may identify the presence of a tachyarrhythmia episode, such as a ventricular fibrillation episode, a ventricular tachycardia episode, or a non-sustained tachycardia (NST) episode. Examples of tachyarrhythmia episodes that may qualify for delivery of responsive therapy include a ventricular fibrillation episode or a ventricular tachyarrhythmia episode. In the case of a NST, however, the count in the interval counters may not meet the requirements for triggering a therapeutic response.

In some examples, processor **90** may operate as an interrupt driven device, and is responsive to interrupts from the pacer timing and control module, where the interrupts may correspond to the occurrences of sensed P-waves and R-waves and the generation of cardiac pacing pulses. Any necessary mathematical calculations to be performed by processor **90** and any updating of the values or intervals controlled by the pacer timing and control module of processor **90** may take place following such interrupts. A portion of memory **92** may be configured as a plurality of recirculating buffers, capable of holding series of measured intervals, which may be analyzed by processor **90** in response to the occurrence of a pace or sense interrupt to determine whether heart **14** of patient **12** is presently exhibiting atrial or ventricular tachyarrhythmia.

In some examples, an arrhythmia detection method may include any suitable tachyarrhythmia detection algorithms. In one example, processor **90** may utilize all or a subset of the rule-based detection methods described in U.S. Pat. No. 5,545,186 to Olson et al., entitled, "PRIORITIZED RULE BASED METHOD AND APPARATUS FOR DIAGNOSIS AND TREATMENT OF ARRHYTHMIAS," which issued on Aug. 13, 1996, or in U.S. Pat. No. 5,755,736 to Gillberg et al., entitled, "PRIORITIZED RULE BASED METHOD AND APPARATUS FOR DIAGNOSIS AND TREATMENT OF ARRHYTHMIAS," which issued on May 26, 1998. U.S. Pat. No. 5,545,186 to Olson et al. and U.S. Pat. No. 5,755,736 to Gillberg et al. are incorporated herein by reference in their entireties. However, other arrhythmia detection methodologies may also be employed by processor **90** in other examples.

In the examples described herein, processor **90** may identify the presence of an atrial or ventricular tachyarrhythmia episode by detecting a series of tachyarrhythmia events

(e.g., R-R or P-P intervals having a duration less than or equal to a threshold) of an average rate indicative of tachyarrhythmia or an unbroken series of short R-R or P-P intervals. The thresholds for determining the R-R or P-P interval that indicates a tachyarrhythmia event may be stored within memory **92** of ICD **16**. In addition, the number of tachyarrhythmia events that are detected to confirm the presence of a tachyarrhythmia episode may be stored as a number of intervals to detect (NID) threshold value in memory **92**. In some examples, processor **90** may also identify the presence of the tachyarrhythmia episode by detecting a variability of the intervals between tachycardia events. For example, if the interval between successive tachyarrhythmia events varies by a particular percentage or the differences between the coupling intervals are higher than a given threshold over a predetermined number of successive cycles, processor **90** may determine that the tachyarrhythmia is present.

If processor **90** detects an atrial or ventricular tachyarrhythmia based on signals from sensing module **96**, and an anti-tachyarrhythmia pacing regimen is desired, timing intervals for controlling the generation of anti-tachyarrhythmia pacing therapies by stimulation generator **94** may be loaded by processor **90** into the pacer timing and control module to control the operation of the escape interval counters therein and to define refractory periods during which detection of R-waves and P-waves is ineffective to restart the escape interval counters.

If ICD **16** is configured to generate and deliver defibrillation pulses to heart **14**, stimulation generator **94** may include a high voltage charge circuit and a high voltage output circuit. In the event that generation of a cardioversion or defibrillation pulse is required, processor **90** may employ the escape interval counter to control timing of such cardioversion and defibrillation pulses, as well as associated refractory periods. In response to the detection of atrial or ventricular fibrillation or tachyarrhythmia requiring a cardioversion pulse, processor **90** may activate a cardioversion/defibrillation control module, which may, like pacer timing and control module, be a hardware component of processor **90** and/or a firmware or software module executed by one or more hardware components of processor **90**. The cardioversion/defibrillation control module may initiate charging of the high voltage capacitors of the high voltage charge circuit of stimulation generator **94** under control of a high voltage charging control line.

Processor **90** may monitor the voltage on the high voltage capacitor, e.g., via a voltage charging and potential (VCAP) line. In response to the voltage on the high voltage capacitor reaching a predetermined value set by processor **90**, processor **90** may generate a logic signal that terminates charging. Thereafter, timing of the delivery of the defibrillation or cardioversion pulse by stimulation generator **94** is controlled by the cardioversion/defibrillation control module of processor **90**. Following delivery of the fibrillation or tachycardia therapy, processor **90** may return stimulation generator **94** to a cardiac pacing function and await the next successive interrupt due to pacing or the occurrence of a sensed atrial or ventricular depolarization.

Stimulation generator **94** may deliver cardioversion or defibrillation pulses with the aid of an output circuit that determines whether a monophasic or biphasic pulse is delivered, whether housing electrode **68** serves as cathode or anode, and which electrodes are involved in delivery of the cardioversion or defibrillation pulses. Such functionality may be provided by one or more switches or a switching module of stimulation generator **94**.

Telemetry module **98** includes any suitable hardware, firmware, software or any combination thereof for communicating with another device, such as INS **26** or programmer **24** (FIG. **1**). Under the control of processor **90**, telemetry module **98** may receive downlink telemetry from and send uplink telemetry to programmer **24** with the aid of an antenna, which may be internal and/or external. Processor **90** may provide the data to be uplinked to programmer **24** and the control signals for the telemetry circuit within telemetry module **98**, e.g., via an address/data bus. In some examples, telemetry module **98** may provide received data to processor **90** via a multiplexer.

In some examples, processor **90** may transmit atrial and ventricular heart signals (e.g., ECG signals) produced by atrial and ventricular sense amp circuits within sensing module **96** to programmer **24**. Programmer **24** may interrogate ICD **16** to receive the heart signals. Processor **90** may store heart signals within memory **92**, and retrieve stored heart signals from memory **92**. Processor **90** may also generate and store marker codes indicative of different cardiac episodes that sensing module **96** detects, and transmit the marker codes to programmer **24**. An example pacemaker with marker-channel capability is described in U.S. Pat. No. 4,374,382 to Markowitz, entitled, "MARKER CHANNEL TELEMETRY SYSTEM FOR A MEDICAL DEVICE," which issued on Feb. 15, 1983 and is incorporated herein by reference in its entirety.

The various components of ICD **16** are coupled to power source **100**, which may include a rechargeable or non-rechargeable battery. A non-rechargeable battery may be selected to last for several years, while a rechargeable battery may be inductively charged from an external device, e.g., on a daily or weekly basis. Examples of a rechargeable battery include, but are not limited to, a lithium ion battery, a lithium polymer battery or a supercapacitor.

In some examples, data from sensing module **96** may be uploaded to a remote server, from which a clinician or another user may access the data to determine whether a potential sensing integrity issue exists. An example of a remote server includes the CareLink Network, available from Medtronic, Inc. of Minneapolis, Minn.

Telemetry module **98** may also be useful for communicating with INS **26**, which may also include a telemetry module as described with respect to FIG. **7**. In some examples, INS **26** and ICD **16** may communicate with each other by way of RF communication techniques supported by the respective telemetry modules. In addition to or instead of the RF communication techniques, INS **26** and ICD **16** may communicate with each other by generating electrical communication signals that are sensed via the other device.

An example of a suitable communication technique for exchanging information between ICD **16** and INS **26** is described in commonly-assigned U.S. Pat. No. 4,987,897 to Funke, which is entitled, "BODY BUS MEDICAL DEVICE COMMUNICATION SYSTEM," and issued on Jan. 29, 1991 and is incorporated herein by reference in its entirety.

FIG. **7** is a functional block diagram of an example INS **26**. INS **26** includes processor **110**, memory **112**, stimulation generator **114**, switching module **116**, telemetry module **118**, sensing module **119**, and power source **120**. In the example shown in FIG. **7**, processor **110**, memory **112**, stimulation generator **114**, switching module **116**, telemetry module **118**, sensing module **119**, and power source **120** are enclosed within outer housing **122**, which may be, for example a hermetic housing. As shown in FIG. **7**, stimulation generator **114** is coupled to lead **28** either directly or indirectly (e.g., via a lead extension). Alternatively, stimulation generator

114 may be coupled to more than one lead directly or indirectly (e.g., via a lead extension, such as a bifurcating lead extension that may electrically and mechanically couple to two leads) as needed to provide neurostimulation therapy to patient 12. Similarly, as shown in FIG. 7, sensing module 119 is coupled to lead 31 directly or indirectly (e.g., via a lead extension). Alternatively, sensing module 119 may be couple to more than one lead directly or indirectly as needed to sense one or more physiological parameters of patient that may be used to detect the EMD state of heart 14, as described herein. The physiological parameters may indicate whether heart 14 is providing sufficient cardiac output. The lack of sufficient cardiac output combined with an electrical cardiac signal that indicates heart 14 is in a sinus rhythm may indicate patient 12 is in an EMD state.

In the example illustrated in FIG. 7, lead 28 includes electrodes 124A-124D (collectively referred to as "electrodes 124"). Electrodes 124 may comprise ring electrodes. In other examples, electrodes 124 may be arranged in a complex electrode array that includes multiple non-contiguous electrodes at different angular positions about the outer circumference of lead 28, as well as different levels of electrodes spaced along a longitudinal axis of lead 28. The configuration, type, and number of electrodes 124 illustrated in FIG. 7 are merely exemplary. In other examples, INS 26 may be coupled to any suitable number of leads with any suitable number and configuration of electrodes. Moreover, lead 28 may comprise a shape other than a cylindrical shape. As an example, lead 28 may comprise a paddle-shaped portion that carries electrodes 124.

Memory 112 includes computer-readable instructions that, when executed by processor 110, cause INS 26 to perform various functions. Memory 112 may include any volatile, non-volatile, magnetic, optical, or electrical media, such as a RAM, ROM, NVRAM, EEPROM, flash memory, or any other digital media. Memory 112 may store therapy programs, which may be stored in therapy program groups, and operating instructions. The therapy programs may define a particular program of therapy in terms of respective values for electrical stimulation parameters, such as electrode combination, electrode polarity, current or voltage amplitude, pulse width and pulse rate. A program group may comprise a plurality of therapy programs that may be delivered together on an overlapping or non-overlapping basis. The stored operating instructions may guide the general operation of INS 26 under control of processor 110, and may include instructions for measuring the impedance of electrodes 124.

Stimulation generator 114 generates stimulation signals, which may be pulses as primarily described herein, or continuous time signals, such as sine waves, for delivery to patient 12 via selected combinations of electrodes 124. Processor 110 controls stimulation generator 114 according to stored therapy programs and/or program groups in memory 112 to apply particular stimulation parameter values specified by one or more of programs, such as amplitude, pulse width, and pulse rate. Processor 110 may include any one or more microprocessors, controllers, a DSPs, ASICs, FPGAs, or equivalent discrete or integrated digital or analog logic circuitry, and the functions attributed to processor 110 herein may be embodied as software, firmware, hardware or any combination thereof.

Processor 110 may also control switching module 116 to apply the stimulation signals generated by stimulation generator 114 to selected combinations of electrodes 124. In particular, switching module 116 couples stimulation signals to selected conductors within leads 28 which, in turn, deliver the stimulation signals across selected electrodes 124. Switching module 116 may be a switch array, switch matrix, multiplexer, or any other type of switching device suitable to selectively couple stimulation energy to selected electrodes. Hence, stimulation generator 114 is coupled to electrodes 124 via switching module 116 and conductors within leads 28. In some examples, INS 26 does not include switching module 116.

Stimulation generator 114 may be a single or multichannel stimulation generator. In particular, stimulation generator 114 may be capable of delivering a single stimulation pulse, multiple stimulation pulses, or a continuous signal at a given time via a single electrode combination or multiple stimulation pulses at a given time via multiple electrode combinations. In some examples, however, stimulation generator 114 and switching module 116 are configured to deliver multiple channels on a time-interleaved basis. In this case, switching module 116 serves to time division multiplex the output of stimulation generator 114 across different electrode combinations at different times to deliver multiple programs or channels of stimulation energy to patient 12.

Sensing module 119 may sense one or more physiological parameters of patient 12 via sensor 121 of lead 31. As described in greater detail below, the one or more physiological parameters of patient 12 sensed by sensing module 119 may include physiological parameters appropriate for determining if heart 14 is in an EMD state. For example, sensor module 119 may be configured to sense one or more physiological parameters indicative of mechanical contraction of heart 14 via sensor 121. In some examples, sensing module 119 senses one or more of blood pressure and blood flow via sensor 121. Blood flow and blood pressure may change as a function of mechanical contraction of heart 14. A blood pressure or blood flow through heart 14 or other vasculature (e.g., blood vessels or arteries) that falls below a particular threshold or decreases by a particular rate may indicate that heart 14 is not sufficiently contracting.

Other physiological parameters indicative of mechanical contraction of heart 14 includes tissue perfusion or blood oxygen saturation. Tissue perfusion and blood oxygen saturation may be sensed using any suitable technique, such as an optical perfusion sensor, a pulse oximeter, or a blood pressure pulse (e.g., a palpitation) detector. A pulse or palpitation detector can be, for example, by a sensor that detects rapid changes in perfusion that occur during a normal heart beat cycle, such as, e.g., an optical perfusion sensor, or a pressure or strain gauge sensor that detects blood vessel dilation/contraction. An optical perfusion sensor may detect general perfusion state associated with adequate heart function or inadequate heart function, or the optical perfusion sensor may detect relatively rapid changes in tissue perfusion that occur during a heartbeat that is pulsatile, thereby indicating some level of mechanical contraction of heart 14 is present. In some examples, an optical perfusion sensor, pulse oximeter, or blood pressure pulse detector may be positioned at a remote location from that of heart 14 and/or may be located at or adjacent to the housing of an IMD, such as, e.g., the housing of IMD 16 or IMD 26.

Example systems and techniques for monitoring tissue perfusion may include those described in U.S. patent application Ser. No. 11/963,045, entitled "OPTICAL SENSOR AND METHOD FOR DETECTING A PATIENT CONDITION," and filed Dec. 21, 2007, the entire content of which is incorporated herein by reference. As described, in some examples, tissue perfussion may be monitored using a light source emitting a light signal and light detector receiving emitted light scattered by the volume of body tissue. The

light dector emits a signal having an alternating current (AC) component corresponding to the pulsatility of blood flow in the body tissue volume. In response to the AC component of the light detector signal, a processor may determine a patient condition (e.g., a heart rhythm). In some examples, a pulsatility metric may be to detected heart rate of a patient. The heart rate detected by the pulsatility metric may be compared to a heart rate determined based on monitored electrical signals (e.g., ECG) of a heart to confirm the heart rate indicated by the electrical signals. Using such a technique, tissue perfusion and/or pulsatility may be monitored to detect an EMD state of heart **14**, e.g., an EMD state may be detected when the rate indicated by the pulsatility is consistent with lack of physiological significant mechanical contractions of heart **14** but the electrical activity of heart **14**, e.g., ECG/EEG signals, during approximately the same time period is indicative of mechanical contraction of heart **14**.

Various hemodynamic characteristics may be derived from relative changes in a blood oxygen saturation level or tissue perfusion of a patient, such as, e.g., relative changes in the blood pressure of the patient or the relative blood flow through a particular blood mass (e.g., a blood vessel or other vasculature), the presence of an acceptable blood flow pulse and/or the presence of palpitation. Therefore, blood oxygen saturation levels may be useful for determining whether heart **14** is contracting in a physiologically significant manner.

Additionally, in some examples, sensing module **119** senses electrical activity of heart **14** via sensor **121**. Accordingly, sensor **121** may be any suitable type sensor capable of sensing the desired physiological parameter. In some examples, sensor **121** communicates parameter information to sensing module **119** via a wired connection, e.g., via lead **31**. Alternatively, sensor **121** may communicate sensed parameter information to sensing module via a wireless connection, in which case sensor **121** may be physically separate from housing **122** and lead **31** may be eliminated from the therapy system. Sensing module **119** may communicate sensed physiological parameter information to processor **110**, which may analyze the parameter information to determine if heart **14** is in an EMD state.

Sensing module **119** may also sense electrical activity of heart **14** and/or one or more nerves of patient **12**. The sensed electrical activity may be used by processor **110** or other processor to evaluate autonomic nervous system activity, e.g., autonomic nervous system activity associated with an EMD state. Therapy delivered to patient **12** to treat an EMD state may be configured based on the autonomic activity associated with the EMD state. In general, as will be described further below, the delivered therapy may be configured to modulate autonomic activity in a manner determined to be appropriate (e.g., by processor **90** or processor **110**) in view of the autonomic nervous system activity determined to be associated with an EMD state.

Telemetry module **118** supports wireless communication between INS **26** and ICD **16**, as well as between INS **26** and an external programmer **24** (FIG. **1**) or another computing device under the control of processor **110**. Telemetry module **118** may also support wireless communication between sensing module **119** of INS **26** and sensor **121** in examples in which sensor **121** is physically separate from INS **26**. Processor **110** of INS **26** may receive, as updates to programs, values for various stimulation parameters such as amplitude and electrode combination, from programmer **24** via telemetry module **118**. The updates to the therapy programs may be stored within memory **112**.

In some examples, processor **110** may store information associated with the detection and/or treatment of an EMD state for patient **14** in memory **112**. Processor **110** may transmit information associated with the detection and/or treatment with external programmer **24** or other external device via telemetry module **118**. In some examples, processor **110** may communicate with external programmer **24** when an EMD state to alert programmer **24** to the detection, which may then alert a user to the EMD state. In some examples, such communication may occur at or near real-time with the detection of the EMD state or may occur at some later time. Processor **110** may alternatively or additionally communicate whether or not the EMD state has been terminated. In some examples, processor **110** may communicate to external programmer **24** the type of stimulation therapy (e.g., one or more therapy programs) used to treat the EMD state as well as an identification of which stimulation therapy was effective in terminating the EMD state. EGM signals or other electrical activity of heart **14** of patient **12** that is associated with the EMD state and/or response to treatment may also be communicated to programmer **24**. In this manner, programmer **24** may allow a user to be alerted to the occurrence of an EMD state, e.g., as it occurs, to be able to observe how the INS **26** responded to the EMD state, and/or observe the response of patient **12** to the situation.

The various components of INS **26** are coupled to power supply **120**, which may include a rechargeable or non-rechargeable battery. A non-rechargeable battery may be selected to last for several years, while a rechargeable battery may be inductively charged from an external device, e.g., on a daily or weekly basis. In other examples, power supply **120** may be powered by proximal inductive interaction with an external power supply carried by patient **12**.

FIG. **8** is block diagram of an example programmer **24**. As shown in FIG. **6**, programmer **24** includes processor **130**, memory **132**, user interface **134**, telemetry module **136**, and power source **138**. Programmer **24** may be a dedicated hardware device with dedicated software for programming of ICD **16** and INS **26**. Alternatively, programmer **24** may be an off-the-shelf computing device running an application that enables programmer **24** to program ICD **16** and INS **26**. In some examples, separate programmers may be used to program ICD **16** and INS **26**. However, a common programmer **24** that is configured to program both ICD **16** and INS **26** may provide a more streamlined programming process for a user, such as a clinician or patient **12**.

A user may use programmer **24** to select therapy programs (e.g., sets of stimulation parameters), generate new therapy programs, modify therapy programs through individual or global adjustments or transmit the new programs to a medical device, such as ICD **16** or INS **26** (FIG. **1**). The clinician may interact with programmer **24** via user interface **134**, which may include display to present graphical user interface to a user, and a keypad or another mechanism for receiving input from a user.

Processor **130** can take the form one or more microprocessors, DSPs, ASICs, FPGAs, programmable logic circuitry, or the like, and the functions attributed to processor **130** herein may be embodied as hardware, firmware, software or any combination thereof. Memory **132** may store instructions that cause processor **130** to provide the functionality ascribed to programmer **24** herein, and information used by processor **130** to provide the functionality ascribed to programmer **24** herein. Memory **132** may include any fixed or removable magnetic, optical, or electrical media, such as RAM, ROM, CD-ROM, hard or floppy magnetic

disks, EEPROM, or the like. Memory **132** may also include a removable memory portion that may be used to provide memory updates or increases in memory capacities. A removable memory may also allow patient data to be easily transferred to another computing device, or to be removed before programmer **24** is used to program therapy for another patient. Memory **132** may also store information that controls therapy delivery by ICD **16** and INS **26**, such as stimulation parameter values.

Programmer **24** may communicate wirelessly with ICD **16** and INS **24**, such as using RF communication or proximal inductive interaction. This wireless communication is possible through the use of telemetry module **136**, which may be coupled to an internal antenna or an external antenna. An external antenna that is coupled to programmer **24** may correspond to the programming head that may be placed over heart **14**, as described above with reference to FIG. **1**. Telemetry module **136** may be similar to telemetry module **98** of ICD **16** (FIG. **6**) or telemetry module **118** of INS **26** (FIG. **7**).

Telemetry module **136** may also be configured to communicate with another computing device via wireless communication techniques, or direct communication through a wired connection. Examples of local wireless communication techniques that may be employed to facilitate communication between programmer **24** and another computing device include RF communication according to the 802.11 or Bluetooth specification sets, infrared communication, e.g., according to the IrDA standard, or other standard or proprietary telemetry protocols. In this manner, other external devices may be capable of communicating with programmer **24** without needing to establish a secure wireless connection.

Power source **138** delivers operating power to the components of programmer **24**. Power source **138** may include a battery and a power generation circuit to produce the operating power. In some examples, the battery may be rechargeable to allow extended operation. Recharging may be accomplished by electrically coupling power source **138** to a cradle or plug that is connected to an alternating current (AC) outlet. In addition or alternatively, recharging may be accomplished through proximal inductive interaction between an external charger and an inductive charging coil within programmer **24**. In other examples, traditional batteries (e.g., nickel cadmium or lithium ion batteries) may be used. In addition, programmer **24** may be directly coupled to an alternating current outlet to power programmer **24**. Power source **138** may include circuitry to monitor power remaining within a battery. In this manner, user interface **134** may provide a current battery level indicator or low battery level indicator when the battery needs to be replaced or recharged. In some cases, power source **138** may be capable of estimating the remaining time of operation using the current battery.

FIG. **9** is a flow diagram illustrating an example technique for delivering electrical stimulation to a patient **12** when heart **14** is in an EMD state. For purposes of illustration, the example techniques of FIGS. **9-14** are described with respect to patient **12** and therapy system **10** of FIG. **2**. However, examples are not limited to such a configuration of therapy system **10**, but instead may be applied to any system or device, e.g., a system or device that is configured to determine that heart **14** is in an EMD state based on one or more sensed physiological signals, and deliver electrical stimulation to any appropriate tissue site to modulate afferent nerve activity and/or inhibit efferent nerve activity when it is determined that heart **14** of patient **12** is in an EMD state, as described herein.

As indicated by FIG. **9**, in some examples, INS **26** senses at least one physiological parameter of patient **12** (**140**), e.g., via sensor **121** (FIG. **7**) of lead **31**. Based at least in part on the one or more sensed physiological parameters, processor **110** of INS **26** may determine whether heart **14** is in an EMD state (**142**). For example, INS **26** may determine that that heart **14** is in an EMD state if a sensed physiological parameter other than that of the electrical activity of heart **14**, e.g., blood pressure and/or blood flow, is indicative of the absence of physiologically significant mechanical contractions of heart **14** but the electrical activity of heart **14**, e.g., ECG/EEG signals, during approximately the same time period is indicative of mechanical contraction of heart **14**. Such an example is further described with respect to FIG. **10** below.

If processor **110** determines that heart **14** is in an EMD state, processor **110** may control stimulation generator **114** to deliver electrical stimulation to a tissue site of patient **12** via selected electrodes **124** of lead **28** in order to modulate afferent nerve activity and/or inhibit efferent nerve activity (**144**). The electrical stimulation delivered by INS **26** may be delivered in manner that results in mechanical contraction of heart **14** to terminate of the EMD state of heart **14**. On the other hand, if processor **110** determines that heart **14** is not in an EMD state, processor **110** may continue monitoring one or more physiological parameters of patient (**140**), which may be indicative of both electrical cardiac activity and mechanical activity of heart **14**.

As previously described, an EMD state may be a condition characterized by the persistence of electrical activity in the heart without associated mechanical contraction or with a relatively low level of mechanical contraction. Accordingly, in some examples, the one or more physiological parameters sensed by INS **26** via sensor **121** may be physiological parameters indicative of the mechanical contraction, or lack thereof, of heart **14**, and sensor **121** may be any suitable type sensor capable of sensing such a desired physiological parameter.

In some examples, physiological parameters that are indicative of mechanical contraction of heart **14** include one or more of blood pressure, blood oxygen saturation level, movement of heart muscles, and blood flow, which may include arterial blood flow, venous blood flow and/or and blood flow in tissue (e.g., tissue perfusion). INS **26** may sense these physiological parameters of patient **12** via sensor **121**. In some examples, sensor **121** includes one or more pressure sensors configured to monitor the blood pressure of patient **12**, e.g., by monitoring pressure within right ventricle **32** or left ventricle **36** (FIG. **1**). As other examples, sensor **121** may include one or more of flow meters, Doppler flow sensors, MRI imaging sensors such as those sensors configured for echo planar imaging (EPI), ion transport sensors, oxygen sensors, pH sensors, blood calcium sensors, blood sugar sensors, piezoelectric sensors, accelerometers, microphones, stress sensors, bend sensors, tissue perfusion sensors and acoustic sensors. Sensor **121** may be located inside heart **14**, on the outer surface of heart **14**, adjacent to heart **14**, and/or other suitable location on or implanted within the body of patient **12**.

Flow meters and/or Doppler flow sensors may monitor arterial and/or venous blood flow rates, which are directly influenced by mechanical contractions of heart **14**. Doppler sensors may also be utilized to measure heart motion to detect insufficient or inappropriate or ineffective heart

motion, which can indicate the failure of heart **14** to sufficiently contract. In a similar manner, an ion transport sensor may monitor blood flow by monitoring the flow of ions contained in the blood of patient **12**, e.g., mineral ions. As another example, one or more oxygen sensors may be used to monitor oxygen levels in the blood of patient **12** as an indicator of mechanical contraction of heart **14**. Generally, blood oxygen saturation levels may increase with contraction of the heart because, as the volume of blood that is output by heart **14** increases, the blood oxygen saturation level typically increases.

In a similar manner, one or more sensors that monitor pH of a patient's blood may be used since the concentration of hydrogen ions in blood of a patient may be correlated with mechanical contraction of heart **14**. For example, a reduction in blood flow may result in a reduction of the pH of the patient's blood. In some examples, a pH sensor may detect acidosis or relatively low pH, which can be at least a part of the reason for the EMD state has occurred or persists. Thus, in some examples, measured pH of a patient's blood may be used to detect an EMD state or confirm an EMD state detected, for example, via another sensed physiological parameter.

Blood calcium sensors may be used, e.g., to detect blood calcium concentrations for patient **12**. If sufficient calcium is not available, cardiac contractility may suffer and contribute to EMD. Thus, in some examples, measured blood calcium concentration may be used to detect an EMD state or confirm an EMD state detected, for example, via another sensed physiological parameter. Similarly, blood sugar sensors may be used, e.g., to detect blood sugar levels for patient **12**. The presence of hypoglycemia may contribute to an EMD state. Thus, in some examples, measured blood sugar levels may be used to detect an EMD state or confirm an EMD state detected, for example, via another sensed physiological parameter.

Piezoelectric sensors may be used, e.g., to detect blood pressure and/or acceleration associated with pulses through patient **12** (e.g., through a blood mass, such as a blood vessel or artery), both of which may be an indicator of mechanical contraction of heart **14**. Acoustic sensors may also be used by monitoring acoustic signal or sounds generated with blood flow, which is influenced by the mechanical contraction of heart **14**, or to monitor acoustic signal or sounds of one or more contractions of heart **14**.

Furthermore, sensor **121** may be positioned relative to patient **12** to allow INS **26** to monitor the selected physiological parameters. In some examples, sensor **121** may be capable of directly sensing the mechanical contraction of heart **14** by sensing the movement of heart **14** corresponding to mechanical contractions of heart **14**, e.g., via one or more single or multi-axis accelerometers positioned in cardiac tissue of heart **14** or tissue proximate to heart **14**. As another example, one or more accelerometers or other sensors may be location proximate or within blood vessel(s) that are directly connected to heart **14**, such as larger blood vessels such as the pulmonary vein, pulmonary artery, vena cava, aorta, and the like, to detect mechanical contractions of the heart. In some examples, ultrasonic imaging sensors may also be used to provide ultrasonic images of heart **14** that may be used to determine if heart **14** is contracting in a physiological significant manner. An accelerometer or ultrasonic signal may be used to detect an EMD state, for example, using a baseline signal template captured when heart **12** was operating in a non-EMD state, that is subsequently compared to one or more measured signals to determine if the measured signals are consistent with the baseline template. If not consistent with the baseline template, the signals may indicate that an EMD state may be present.

In some examples, electrical activity of heart **14** may be monitored by INS **26** to determine if heart **14** is in an EMD state. For example, sensor **121** coupled to INS **26** may include one or more sense electrodes configured to monitor electrical signals of heart **14**, in conjunction with the one or more physiological parameters indicative of mechanical contraction previously described, in a manner that may be used to determine if heart **14** is in an EMD state. Alternatively, or additionally, in some examples, the electrical activity of heart **14** may be monitored via electrodes on one or more of leads **18**, **20**, **22** coupled to ICD **16**, which may monitor the same or similar electrical activity of heart **14** to properly deliver of at least one of pacing, cardioversion, or defibrillation therapy to heart **14** of patient **12**. In such examples, ICD **16** may communicate information regarding the sensed electrical activity of heart **14** to INS **26**, e.g., via the respective telemetry modules **98** and **118**, so that INS **26** may determine whether heart **14** is in an EMD state. As will be described below, the electrical activity of heart sensed by INS **26** and/or ICD **16** may be analyzed in conjunction with the corresponding physiological parameters to determine whether or not heart **14** is exhibiting normal electrical activity, at least to the extent that the electrical activity may be typical to that of a heart in an EMD state **14**.

In one example, INS **26** may monitor the peak endocardial interval (PEI) using sensor **121** to determine whether heart **14** is in an EMD state. The PEI may be characterized as the time between the peak of an electrical signal of heart **14** (e.g., such as the Q peak of the QRS complex) and the peak magnitude of the acceleration of heart **14**, e.g., as measure by an accelerometer sensor. In general, the PEI interval normally is about 150 milliseconds to about 250 milliseconds after the Q peak of the QRS complex for a heart that is contracting in a physiologically significant manner. In cases in which heart **14** is in an EMD state, the PEI interval may be outside the normal PEI interval, for example, due to the failure of heart to mechanically contract, thereby increasing the PEI interval.

In some examples, INS **26** (or other device) may monitor the respiration of patient **12** to determine whether heart **14** is in an EMD state. Hypoxia secondary to respiratory failure may be a cause of an EMD state, and respiratory insufficiency can be present during the occurrence of an EMD state. Accordingly, INS **26** may be configured to monitor for instances of respiratory insufficiency, acute respiratory arrest or other respiratory condition associated with EMD to at least in part detect when heart **14** is in an EMD state. In some example, respiratory insufficiency and/or acute respiratory arrest may be used to confirm the identification of an EMD state based on one or more other physiological parameters.

INS **26** and/or ICD **16** may monitor respiration parameters, such as the rate profile of inhalation and/or exhalation and the respiration rate, by sensing thoracic impedance to determine if patient **12** is breathing normally or abnormally. Normal breathing or abnormal breathing can be indicated by, for example, a threshold respiration rate or a threshold range of respiration rates, or by a template that indicates a profile of inhalation and exhalation patterns that is normal or abnormal (e.g., indicative of the possible presence of an EMD state). In some examples, INS **26** may control stimulation generator **114** (FIG. **7**) to deliver stimulation to patient **12** to treat an EMD state if patient **12** is breathing abnormally. In some example, INS **26** may apply the electrical stimulation to treat EMD if patient is breathing abnormally

in conjunction with the determination that another physiological parameter of patient is indicative of heart **14** being in an EMD state.

Processor **110** or other processor of another device may analyze sensed physiological parameter information to determine whether heart **14** is in an EMD state. For example, processor **110** may analyze the sensed physiological parameter information using one or more suitable algorithms configured to detect an EMD state based on sensed parameter information. In some examples, a detection algorithm may weight one or more patient factors that may increase or decrease the overall likelihood of heart **14** of patient **12** being in an EMD state. Such patient factors may include the age and/or gender of patient **12**. For example, the algorithm can reflect the possibility that heart **14** may be more likely to enter an EMD state in cases in which patient **12** is a female. As another example, the algorithm can increase the possibility that a particular physiological parameter indicates heart **14** is in an EMD state based on the age of patient **12**; heart **14** may be more likely to enter an EMD state with increased age of patient **12**. For example, EMD of heart **14** may by more likely to occur in a patient that is older than, e.g., seventy years of age compared to that of patient **12** that is younger than seventy years of age.

Accordingly, the detection algorithm applied by processor **110** (e.g., by executing one or more machine readable instructions stored in memory **112** of INS **26**) may incorporate patient factors of patient **12** that may increase or decrease the likelihood of heart **14** entering an EMD state. Such factors may be taken into account, for example, in cases in which sensed physiological parameter and other information analyzed by processor **110** indicate a borderline determination of an EMD state of patient, e.g., a determination that there is a small probability that a particular physiological parameter indicates the EMD state is occurring. For example, if a borderline EMD state determination is made and one or more patient factors, such as age or sex, reflect an increased likelihood of heart **14** entering an EMD state, then processor **110** may determine that heart **14** is in an EMD state. Conversely, if a borderline EMD state determination is made and one or more patient factors, such as age or sex, do not reflect an increased likelihood of heart **14** entering an EMD state, then processor **110** may determine that heart **14** is not in an EMD state. A clinician can adjust the EMD state detection algorithm according to the factors known to the clinician to better indicate whether a particular physiological parameter indicates heart **14** of patient **12** is in an EMD state.

Although sensor **121** is shown to be positioned within or proximate to heart **14** of patient **12** in the examples of FIGS. **1** and **2**, in other examples, sensor **121** may have any suitable position relative to heart **14**. Sensor **121** may positioned at any suitable location with respect to patient **12** that allows sensor **121** to properly monitor one or more desired physiological parameters that are indicative of mechanical contraction of heart **14**. Furthermore, in some examples, sensor **121** is implanted within patient **12**, e.g., as shown in the examples of FIGS. **1** and **2**. In other examples, sensor **121** is located external to patient **12** in a position that allows sensor **121** to monitor the desired physiological parameter. As one example, a sensor **121** that monitors the pulse of patient **12** may be incorporated into a wristband that may be worn on the wrist of patient **12**, e.g., in the same manner as a wrist watch.

INS **26** may deliver electrical stimulation to modulate afferent nerve activity of patient **12** by configuring the electrical stimulation to modify the afferent nerve activity of patient **12**. For example, stimulation generator **114** (FIG. **7**) of INS **26** may deliver electrical stimulation that is configured to excite an afferent nerve activity of a nerve of patient **12** and/or inhibit afferent nerve activity. In general, afferent nerve activity includes nerve impulses sent from receptors or sense organs to the central nervous system, e.g., the brain and spinal cord, via afferent nerve pathways. Such nerve impulses may be associated with the sensory function of the nervous system patient by providing information to the central nervous system brain gathered via the peripheral nervous system.

By modulating afferent nerve activity via delivery of electrical stimulation when it is determined that patient **12** is in an EMD state, the EMD state may be treated without delivering electrical stimulation that directly excites efferent nerve activity within efferent nerve pathways associated with heart **14** of patient **12**. Instead, the EMD state may be treated by directly modulating the nerve impulses that are sent to the brain of patient **12** via electrical stimulation rather than those sent from the brain. In turn, depending on the nature of the afferent nerve activity modulation, the patient's brain may react to the modulated afferent nerve activity in a manner that treats (e.g., helps terminate) the EMD state of the heart, e.g., by causing sufficient mechanical contraction of heart **14**. Treating an EMD state of heart **14** may include, for example, increasing the mechanical contraction of heart **14**.

In some examples, delivery of electrical stimulation to inhibit afferent nerve activity may act to prevent the delivery of certain impulses to the brain of patient **12** via afferent pathways. In the absence of such afferent nerve impulse, the brain may react in a manner that helps treat the EMD state. For example, in the absence of such impulses, the brain may react by sending one or more impulses to heart **14** via efferent nerve pathways in a manner that results in the increased mechanical contraction of heart **14**.

Furthermore, in some examples, delivery of electrical stimulation by INS **26** to excite afferent nerve activity of patient **12** may promote the delivery of certain impulses to the brain via afferent pathways. In the presence of such afferent nerve impulses, the brain of patient **12** may react in a manner that effectively treats the EMD state. For example, in the presence of such impulses, the brain may again react by sending one or more impulses to heart **14** via efferent nerve pathways in a manner that results in the increased mechanical contraction of heart **14**.

Alternatively, or in addition to the modulation of afferent nerve activity, the electrical stimulation may be delivered to patient **12** to inhibit efferent nerve activity when it is determined that heart **14** of patient **12** is in an EMD state. Efferent nerve activity includes nerve impulses sent from the central nervous system to effectors, e.g., muscles or glands, via efferent nerve pathways. Such nerve impulses may be associated with the motor function of patient **12**, including muscular control, by providing a mechanism for the brain to communicate with the effectors.

By inhibiting efferent nerve activity via delivery of electrical stimulation when it is determined that patient **12** is in an EMD state, the EMD state may be treated without delivering electrical stimulation that directly excites efferent nerve activity within efferent nerve pathways associated with heart **14** of patient **12**. Instead, the EMD state of heart **14** may be treated by directly inhibiting nerve impulses that have been sent from the brain of patient **12**, or central nervous system in general, via efferent pathways to heart **14**. In turn, the inhibition of the efferent nerve activity from the

electrical stimulation may result in mechanical contraction of heart **14** to effectively treat the detected EMD state.

INS **26**, via electrodes of lead **28**, may deliver electrical stimulation to one or more tissue sites that allow for the modulation of afferent nerve activity and/or inhibition of efferent nerve activity, as described above. For example, INS **26** and lead **28** may deliver electrical stimulation to a nonmyocardial tissue site and/or a nonvascular cardiac tissue site to modulate afferent nerve activity and/or inhibit efferent nerve activity. In some examples, INS **26** and lead **28** may deliver electrical stimulation to one or more tissue sites proximate one or more afferent nerves or nerve bundles, e.g., in examples in which the delivery of electrical stimulation modulates afferent nerve activity. In other examples, INS **26** and lead **28** may deliver electrical stimulation to one or more tissue sites proximate one or more efferent nerves or nerve bundles, e.g., in examples in which the delivery of electrical stimulation inhibits efferent nerve activity. In still other examples, electrical stimulation may be delivered to the median nerve, vagal nerve, cardiac sympathetic nerve, and/or subcutaneous tissue that contains nerve fibers/sensors in order to modulate afferent nerve activity and/or inhibit efferent nerve activity.

In some examples, the tissue site of patient **12** to which INS **26** delivers the electrical stimulation when the EMD state of heart **14** is detected is a tissue site other than myocardial tissue of heart **14**. Myocardial tissue of heart **14** may be the target tissue of pacing, cardioversion, and/or defibrillation therapy delivered by ICD **16**. Accordingly, in some examples, INS **26** does not deliver electrical stimulation directly to tissue of heart **14**. Despite the fact that the electrical stimulation is not delivered directly to a myocardial tissue site of heart, or even a noncardiac tissue site in general, the electrical stimulation delivered by INS **26** may help treat the EMD state of heart **14** by increasing the contraction of heart **14** such that the contraction of heart **14** and electrical cardiac signals are appropriately synchronized). In this manner, INS **26** may be utilized to treat an EMD state of heart **14**.

In some examples, electrodes **124** of lead **28** may be positioned to deliver electrical stimulation to one or more sites proximate to spinal cord **44** (FIG. **2**). For example, INS **26** may deliver electrical stimulation via lead **28** proximate to one or more vertebrae of patient **12**. As another example, electrical stimulation may be delivered to a site proximate to one or more of thoracic segments, including thoracic segments T1-T6. For example, electrical stimulation may be delivered proximate to one or more of thoracic segments T3, T4, T5 and/or T6, including across one or more of the spans from T3 to T6, T4 to T6, and T1 to T6. In other examples, INS may deliver electrical stimulation via lead **28** to peripheral nerve locations in communication with spinal cord **44**. By delivering electrical stimulation to one more of the above locations, afferent nerve activity may be modulated and/or efferent nerve activity may be inhibited in a manner that results in one or more mechanical contractions of heart **14** when in an EMD state.

INS **26** may generate and deliver electrical stimulation according to one or more therapy programs stored in memory **112** (FIG. **7**) that define one or more parameters of appropriate electrical stimulation. In some examples, the pulse rate of the electrical stimulation signals delivered to patient **12** to treat the EMD state of the patient may range from approximately 1 Hz to approximately 200 Hz, such as, e.g., approximately 10 Hz to approximately 1 kilohertz. Additionally, example electrical stimulation signals may have a voltage ranging from approximately 0.2 volts to approximately 12 volts, such as, e.g., approximately 0.5 volts to approximately 10 volts. Example pulse width of the electrical stimulation signals may range from approximately 0.1 milliseconds to approximately 5 milliseconds, such as, e.g., 0.2 milliseconds. Other stimulation parameter values are contemplated.

In general, INS **26** may generate and deliver electrical stimulation the tissue site of patient **12** for a duration of time that is appropriate for terminating an EMD state of heart **14**. The duration of time for delivery of electrical stimulation by INS **26** may less than the amount of time for the EMD state to be harmful to patient **12**. In some examples, INS **26** is configured to generate and deliver electrical stimulation to the tissue site within a minimal amount of time after INS **26** has successfully determined that heart **14** is in an EMD state. For example, INS **26** may be configured to deliver electrical stimulation to the tissue site substantially immediately after INS **26** has successfully determined that heart **14** is in an EMD state. In some examples, INS **26** may be configured to delivery electrical stimulation to the tissue site of patient **12** between approximately 1 second to approximately 30 minutes after determining that heart **14** is in an EMD state.

In some examples, INS **26** may be configured to both determine heart **14** is in an EMD state and deliver electrical stimulation to the tissue site of patient **12**, as previously described, within approximately 1 millisecond to approximately 30 seconds, such as, e.g., approximately 30 milliseconds to approximately 30 seconds, of heart **14** entering an EMD state. As will be described in greater details below with respect to FIG. **12**, heart **14** may enter an EMD state after the delivery of cardioversion or defibrillation therapy to heart **14** via ICD **26**. In such cases, INS **16** may determine if heart **14** is in an EMD state and deliver stimulation to the tissue site of patient **12**, as previously described, within approximately 1 second to approximately 30 seconds, such as, e.g., approximately 5 second to approximately 30 seconds, of ICD **26** delivering cardioversion or defibrillation therapy.

In the event that the initial therapy delivered to patient **12** from INS **26** does not result in resolution of the EMD state, then processor **110** (FIG. **7**) may be configured to sequentially run through a series of therapy programs, e.g., defining different stimulation signals, electrode combinations, and electrode locations, in an attempt to identify a therapy that is effective in terminating the EMD state of heart **14** and/or a more efficacious therapy for treating EMD. In some examples, INS **26** may deliver stimulation according to each program for between approximately 5 seconds to approximately 60 seconds. If a therapy is found to be effective in terminating the EMD state, INS **26** may continue with that therapy program until the EMD state is fully mitigated (e.g., heart **14** begins mechanically contracting in a physiologically significant manner) or may continue the therapy beyond initial mitigation. In some examples, INS **26** may continue to delivery therapy to patient **12** for approximately 30 seconds to approximately 120 minutes after the EMD state has been terminated as a follow-up therapy to help assure that EMD state does not imminently reappear. The stimulation therapy delivered by INS **26** can initiate at a relatively large amplitude or duty cycle "on" time to treat an EMD state. Then, after EMD is resolved, the stimulation therapy may be adjusted, e.g., to remain at a lower amplitude and/or duty cycle. In other examples, however, after a detected EMD state is addressed and INS **26** determines that heart **14** is mechanically contracting in a physiologically significant manner (e.g., using techniques described above

or by receiving an indication from INS **26**), INS **26** may discontinue all therapy delivery to patient **12** until another EMD state is detected.

In some examples, INS **26** may delivery therapy to patient **12** on a continuous or periodic basis to treat one or more other patient conditions. As such, INS **26** in not limited to delivery of stimulation to patient **12** upon the detection of an EMD state. In some examples, the stimulation therapy may include stimulation that modulates afferent nerve activity or inhibits efferent nerve activity, even in cases in which an EMD state is not detected. Stimulation therapy may be delivered to patient alternately between low intensity/duty cycle and high intensity/duty cycle, as a means to avoid habituation and reduction in therapeutic efficacy. In these examples, INS **26** can adjust the timing of therapy delivery, one or more stimulation parameter values or the target therapy delivery site based on the detection of an EMD state. The EMD therapy can be delivered in conjunction with or instead of the other therapy delivered by INS **26** to manage other patient conditions.

As described below, in some examples, INS **26** delivers stimulation to treat an EMD state in conjunction with the delivery of a cardioversion or defibrillation signal from ICD **12**. The EMD stimulation may be initiated or increased after each cardioversion or defibrillation signal or may be delivered before and/or during a cardioversion or defibrillation signal to help prevent EMD, which can occur after the delivery of a cardioversion or defibrillation shock or otherwise be associated with such therapy. In some examples, INS **26** may sense the delivery of a cardioversion or defibrillation therapy. For example, INS **26** may anticipate the delivery of a cardioversion or defibrillation therapy based on a sensed EGM signal that indicates that such therapy is needed. As another example, electrodes of leads **28**, **29** may detect defibrillation energy in body of patient **12** or an accelerometer sensor or acoustic/microphone sensor may detect severe mechanical jolt that may accompany the delivery of cardioversion or defibrillation therapy to patient **12**. In such a situation, an accelerometer or acoustic/microphone sensor may be located within housing **122** of INS **26** as it may not be required to be at or near heart **14** to detect such defibrillation or cardioversion therapy. In some examples, ICD **16** may be configured to communicate with INS **26** to indicate imminent, occurring, and/or previously delivered defibrillation or cardioversion therapy. In some examples, for communication regarding stimulation therapy, ICD **16** and INS **26** may utilize one or more example techniques described in U.S. patent application Ser. No. 12/362,768, entitled "IMPLANTABLE MEDICAL DEVICE CROSSTALK EVALUATION AND MITIGATION," and filed Jan. 30, 2009, the entire content of which is incorporated herein by reference. Other example techniques are contemplated.

FIG. **10** is a flow diagram illustrating an example technique for detecting when heart **14** is in an EMD state. As indicated by FIG. **9**, INS **26** may sense at least one physiological parameter of patient **12** via sensor **121** (FIG. **7**) of lead **31** (**140**), as previously described, to determine a value of the parameter. In accordance with the technique shown in FIG. **10**, INS **26** compares the sensed parameter value to a threshold value stored in memory **112** (**148**). In some examples, the threshold value may define a minimum parameter value observed in patient **12** when physiologically significant mechanical contraction of heart **14** is properly occurring. As previously indicated, a physiologically significant mechanical contraction may be, e.g., contractions necessary to supply the cardiac output (e.g., sufficient blood flow) to meet the needs of the patient's body. For example, in the case of blood pressure, the threshold value may define a minimum blood pressure value that is exhibited at the location monitored by sensor when physiologically significant mechanical contractions of heart **14** are present.

If the sensed parameter value is greater than or equal to that of the threshold value, INS **26** determines that mechanical contractions are likely occurring and INS **26** may continue monitoring the physiological parameter (**140**). Alternatively, if the sensed parameter value is less than the threshold value defined for the respective physiological parameter, INS **26** may determine that physiologically significant mechanical contractions of heart **14** are not occurring.

When INS **26** determines that mechanical contractions of heart **14** are not occurring based on the comparison of the physiological parameter to the threshold value, INS **26** subsequently determines whether the electrical activity of heart **14** is normal (**150**). For the purposed of this example, normal electrical activity of heart **14** may refer to electrical cardiac activity, e.g., an electrical cardiac signal indicative of a sinus rhythm, which may persist when heart **14** is in an EMD state.

If the electrical activity of heart **14** is normal electrical cardiac activity and INS **26** determined that heart **14** is not mechanically contracting in a physiologically significant manner, INS **26** may determine that heart **14** is in an EMD state. In such cases, processor **110** (FIG. **7**) of INS **26** may control stimulation generator **114** to deliver electrical stimulation to patient **12**, as described above, to treat the EMD state of heart **14** (**152**), e.g., by causing mechanical contraction of heart **14**. Alternatively, if the electrical activity of heart **14** is abnormal rather than normal, then INS **26** may determine that heart **14** is not in an EMD state but rather in a state in which mechanical contraction and normal electrical activity of heart **14** is not present. In this case, INS **26** may notify ICD **16** that cardiac rhythm therapy is desirable.

In other examples of the technique shown in FIG. **10**, processor **110** of INS **26** determines that heart **14** is not mechanically contracting in a physiologically significant manner, e.g., heart **14** is not providing sufficient output, by determining whether the sensed value of the physiological parameter is greater than or equal to a threshold value.

In addition, in other examples of the technique shown in FIG. **10**, processor **110** of INS **26** determines that heart **14** is not mechanically contracting in a physiologically significant manner by determining whether the sensed value of the physiological parameter falls within a predetermined range of values. In some examples, the predetermined range of values indicates a range of physiological parameter values that are observed when physiological significant mechanical contraction of heart **14** is not present.

If the sensed value is within the range of the threshold value, INS **26** determines that sufficient mechanical contraction of heart **14** is not occurring in patient **12**. In other examples, the predetermined range of values indicates a range of physiological parameter values that are observed when physiological significant mechanical contraction of heart **14** is present. If the sensed value is within the range of threshold value, INS **26** determines that sufficient mechanical contractions of heart **14** are occurring.

In some examples, the threshold parameter value is a mean or median value of the physiological parameter over a range of time, e.g., when heart **14** is known to not be in an EMD state, or a value at a discrete point in time. Alternatively or additionally, the threshold parameter value may define one or more trends of a sensed physiological param-

eter value over time, where the trend indicates a decrease in mechanical activity of heart **14**. The trend may be stored as a value (e.g., a slope that indicate the change in the physiological parameter value over time) or a template signal that indicates the values for the change in the physiological parameter value over time.

For example, the threshold value may a define a specific behavior of the parameter value during a period of blood pressure change, e.g., an increase or decrease in value, over a period of time. The threshold parameter value may indicate whether the blood pressure change was approximately constant over the period of time or whether the blood pressure change included alternating periods of rapid change and leveling off. Furthermore, the threshold values may remain substantially the same throughout the life of the implanted device, or may be updated periodically. For example, the one or more sensed parameters may be continually or periodically monitored by INS **26** to dynamically define an average parameter value for patient **12**, which may be used to determine whether heart **14** is in an EMD state.

Processor **110** may compare a trend in the sensed physiological parameter over time to the threshold value in order to determine whether heart **14** is in an EMD state. In the case of a trend template, if the trend in the sensed physiological parameter over time substantially correlates (e.g., correlates about 75% or greater, although other percentages of correlation may be used) to a stored template, processor **110** may determine that heart **14** is in an EMD state.

FIG. **11** is a flow diagram illustrating another example technique for determining when heart **14** is in an EMD state. The example technique is similar to that of the example technique illustrated in FIG. **10**. However, in the example of FIG. **11**, INS **26** may make a consistency determination based on a second sensed physiological parameter after at first sensed physiological parameter indicates an absence of mechanical contraction of heart **14**. The first and second physiological parameters are different.

As indicated by FIG. **11**, INS **26** senses a first physiological parameter, which may include one of the physiological parameters previously described, e.g., patient blood pressure, to determine a value of the respective parameter (**154**). Processor **110** of INS **26** compares the value of the first physiological parameter to a threshold value stored in memory **112** (**156**). The threshold value may be a first threshold value that is associated with the first physiological parameter. If the sensed value of the first physiological parameter is greater than or equal to the threshold value, then INS **26** may determine that physiologically significant mechanical contractions of heart **14** are present, and continue to monitor the first physiological parameter (**154**).

Alternatively, if the sensed value of the first physiological parameter is less than the first threshold value, processor **110** of determines that mechanical contractions of heart **14** are not occurring. In such a situation, processor **110** determines whether the electrical activity of heart **14** is normal, as described above with respect to FIG. **10** (**156**). If processor **110** determines that the electrical activity of heart **14** is not normal, processor **110** may determine that heart **14** is not is an EMD state, but rather in state in which both mechanical contractions and normal electrical activity are absent. However, if the electrical activity of heart **26** is normal electrical activity, then INS **26** may determination that heart **14** is in an EMD state.

In the example technique shown in FIG. **11**, when INS **26** determines that heart **14** is in an EMD state based on the first sensed parameter, INS **26** does not directly proceed to deliver electrical stimulation to patient **12** to treat the EMD state. Instead, INS **26** determines whether a second physiological parameter indicative of contraction of heart **14** also indicates heart **14** is not contracting in a physiologically significant manner. In this way, processor **110** of INS **26** may make a consistency determination to determine whether a heart **14** is in an EMD state. Thus, after determining heart **14** is in an EMD state based on the first sensed parameter, INS **26** senses a second physiological parameter that is different than the first physiological parameter and determines a value of the respective parameter (**160**). Processor **110** compares the sensed value of the second physiological parameter to a second threshold value stored in memory **112** that corresponds to the second sensed parameter (**162**). The first and second threshold values may be different and can vary depending on the type of physiological parameter.

If the sensed value of the second physiological parameter is greater than or equal to the second threshold value, processor **110** determines that the second physiological parameter value does not indicate heart **14** is in an EMD state. Accordingly, processor **110** determines that the first EMD state determination based on the first sensed physiological parameter is inconsistent with the second EMD state determination based on the second physiological parameter. In such a case, INS **26** withholds delivery of electrical stimulation to patient **12**, and may repeat the process.

On the other hand, if the value of the second physiological parameter is less than the threshold value, processor **110** of INS **26** determines that heart **14** is in an EMD state. Accordingly, processor **110** may determine that the first EMD state determination based on the first sensed physiological parameter is consistent with the second EMD state determination based on the second sensed physiological parameter. Upon determining that heart **14** is in an EMD state based on both the first and second physiological parameters, processor **110** controls stimulation generator **114** to deliver electrical stimulation to a tissue site of patient **12** to modulate afferent nerve activity and/or inhibit efferent nerve activity, as described above, and treat the EMD state of heart **14** (**164**).

The technique shown in FIG. **11** may be a more robust technique for determining that heart **14** is in an EMD state correctly reflects the actual state of heart **14**, and may be useful for increasing the likelihood that the determination that heart **14** is in an EMD state is correct. Although FIG. **11** is described with respect to making two EMD state determinations based on two separate physiological parameters of patient **12**, in other examples, processor **110** of INS **26** may make any suitable number of EMD state determinations based on any suitable number of sensed physiological parameters of patient **12**. For example, INS **26** may monitor more than two types of physiological parameters of patient **12**.

FIG. **12** is a flow diagram illustrating an example technique for monitoring heart **14** for an EMD state relative to delivery of defibrillation therapy to heart **14** by ICD **16**. While the example of FIG. **12** is described with respect to delivery of defibrillation therapy to heart **14**, other examples of the technique may include delivery of a cardioversion therapy to heart **14**. Although not limited to such situations, heart **14** may be susceptible to EMD following the delivery of defibrillation and/or cardioversion therapy to heart **14** by ICD **16**. Accordingly, in some examples, INS **26** may be configured to monitor for an EMD state of heart **14** in conjunction with the delivery of such therapy to heart **14** of patient **12** via ICD **16**.

As indicated by FIG. **12**, ICD **16** delivers defibrillation therapy to patient **12** in the form of electrical stimulation (e.g., a shock) delivered via one or more electrodes on leads **18**, **20**, **22** (**166**). For example, ICD **16** may deliver the therapy based on the determination that heart **14** is in a fibrillation state. While the therapy delivered by ICD **16** may successfully terminate the fibrillation of heart **14**, heart **14** may be susceptible EMD immediately after the delivery of the defibrillation therapy.

INS **26** may detect the delivery of the defibrillation therapy to heart **14** using any suitable technique. In some examples, INS **26** senses the electrical signals associated with the delivery of the defibrillation therapy via one or more electrodes of lead **28** and/or sensor **121** of lead **31**. In other examples, before, during, or after the delivery of a the defibrillation therapy to heart **14**, ICD **16** communicates information indicative of the delivery of the defibrillation therapy to INS **26** via the respective telemetry modules **98**, **118**. In response to detecting the delivery of the defibrillation therapy to heart **14**, processor **110** of INS **26** may determine whether heart **14** is in an EMD state.

In one example, as shown in FIG. **12**, before, during or after delivery of the defibrillation therapy by ICD **16**, INS **26** senses a physiological parameter indicative of the contraction of heart **14**. As previously described, physiological parameters indicative of the contraction of heart **14** include blood pressure, blood flow, blood oxygen saturation level, movement of cardiac muscles, heart sounds, heart images, and tissue perfusion.

In some examples, INS **26** immediately begins sensing the physiological parameters after receiving the indication that ICD **16** delivered the defibrillation therapy or after sensing the delivery of the defibrillation therapy. In other examples, INS **26** may begin sensing the physiological parameters after the passage of an appropriate delay period after the delivery of the defibrillation therapy. For example, such a delay period may correspond to the time generally required for one of more of the physiological parameter sensed by INS **26** to reach a level indicative of the absence of mechanical contraction of heart **14**.

Similar to that described above, if INS **26** determines that heart **14** is in an EMD state (**170**), INS **26** delivers appropriate electrical stimulation to patient **12** to cause the desired mechanical contractions of heart **14** and terminate the EMD state of heart **14** (**172**). On the other hand, if INS **26** does not determine that heart **14** is in an EMD state based on the physiological parameters sensed after the delivery of the defibrillation pulse, INS **26** may stop sensing the physiological parameters (**174**). In some cases, INS **26** may continue to monitor for an EMD state of heart **14** for time period corresponding the period in which heart **14** is likely to enter an EMD state after defibrillation therapy is delivered to heart **14**. In this manner, INS **26** may be configured to monitor the one or more appropriate physiological parameters at times that heart **14** may be most susceptible to being in an EMD state, rather than continuously monitoring patient **12** for an EMD state.

As indicated in FIG. **12**, INS **26** may continue delivering the first stimulation therapy until processor **110** determines heart **14** is no longer in an EMD state. This determination may be made according to the same sensed physiological parameters used to initially determine that heart **14** was in an EMD state. For example, after or during the delivery of the first neurostimulation therapy, processor **110** may determine whether heart **14** of patient **12** is mechanically contracting and whether a relatively normal sinus rhythm is detected. In some examples, INS **26** may deliver the first stimulation therapy to patient **12** substantially continuously. Such an example may correspond to configurations in which an accurate EMD state determination is not prevented by the delivery of the first stimulation therapy to patient **12**, e.g., sensing module **119** may accurately sense the one or more physiological parameters regardless of whether the electrical stimulation is being delivered to the tissue site. In other examples, INS **26** may deliver the first stimulation therapy on a periodic basis rather than substantially continuously, e.g., in configurations in which an accurate EMD state determination is prevented during the delivery of the stimulation therapy by INS **26**. For example, in such cases, INS **26** may deliver the first stimulation therapy to the tissue site for set periods of time with periodic pauses that to allow for an accurate determination as to whether heart **14** is still in an EMD state, or if the EMD state of heart **14** has been successfully treated by the stimulation therapy.

In any case, INS **26** continues to deliver first stimulation therapy to patient **12** until processor **110** determines that heart **14** is no longer in an EMD state based on the one or more sensed physiological parameters (**174**). In this manner, INS **26** may continue to deliver the first stimulation therapy to the tissue site until the sensed physiological parameters indicate that heart **14** is no longer in an EMD state.

Alternatively or additionally, INS **26** may deliver the first stimulation therapy for only a predetermined amount of time. For example, INS **26** may be configured to deliver the first stimulation therapy until a predetermined first time period, which may be defined according to the typical amount of time required to treat heart **14** in an EMD state via the first therapy, has expired or processor **110** determines that heart **14** is no longer in an EMD state. In this manner, INS **26** may be prevented from continuously delivering the first stimulation therapy to the tissue site for an unnecessary length of time in the event of an inaccurate EMD state determination by processor **110** of INS **26**. In examples, electrical stimulation therapy may be delivered to the tissue site of patient **12** to treat EMD for approximately 1 second to approximately 10 minutes. In some examples, INS **26** may continue to deliver stimulation to patient **12** for a predetermined amount of time subsequent to the termination of the EMD state. The predetermined amount of time may be a constant amount of time or may be a function of the amount of time needed to treat the EMD state, e.g., the longer the amount of time need to terminate the EMD state, the longer the amount of time the therapy will be delivered after the EMD state is terminated.

FIG. **13** is a flow diagram illustrating an example technique for monitoring heart **14** for an EMD state relative to delivery of a defibrillation therapy to heart **14** by ICD **16**. The example technique is similar to that previously described with respect to FIG. **12**. For example, ICD **16** may deliver defibrillation therapy to patient **12** in the form of electrical stimulation delivered via one or more electrodes on leads **18**, **20**, **22** (**174**). INS **26** may sense at least one physiological parameter of patient **12** after delivery of the defibrillation therapy (**176**), which may then be used to determine an EMD state of heart **14** (**178**), e.g., as described above with respect to FIG. **10**. In the example shown in FIG. **13**, if the EMD state is detected, processor **110** of INS **26** controls stimulation generator **114** to deliver a first stimulation therapy during a first time period, and then delivering a second stimulation therapy during a second time period, e.g., upon expiration of the first time period.

In particular, when processor **110** of INS **26** determines that heart **14** is in an EMD state (**178**), processor **110** may control stimulation generator **114** to deliver a first stimula-

tion therapy to a tissue site to modulate afferent nerve activity and/or inhibit efferent nerve activity (**180**). In some examples, the first therapy delivered by INS **26** may include relatively high intensity stimulation. Delivery of the high intensity stimulation may be particularly effective in treating the EMD state of heart **14**, e.g., by "waking-up" the brain of patient **12** to the EMD state of heart **14**. In some examples, the first stimulation therapy having a relatively high intensity may be achieved by delivering a stimulation signal comprising a relatively high pulse rate and/or relatively high pulse amplitude. In some examples, the first therapy may have a frequency (e.g., a pulse rate) between approximately 10 to 200 Hz, such as, e.g., 50-100 Hz, although other pulse rates are contemplated. In general, the pulse rate may be set at as high of frequency possible, with consideration to the stimulation limitations of INS **26** and patient **12**. Stimulation amplitude of the first therapy may range from approximately 0.5 volts to approximately 12 volts, such as, e.g., approximately 5 volts to approximately 10 volts or approximately 1 volt to approximately 10 volts, although other stimulation amplitudes are contemplated. In some examples, the amplitude may be approximately equal to the maximum stimulation amplitude tolerable by patient **12**.

While the relatively aggressive first stimulation therapy may be effective in terminating the EMD state of heart **14**, depending on the exact parameters of the first therapy delivered, it may be safe to only deliver the first therapy to the tissue site for a short period of time to avoid one or more undesirable side-effects. For example, in some cases, the first stimulation therapy having a relatively high intensity may stress tissue if the stimulation is delivered for too long. Accordingly, INS **26** may be configured to deliver the first stimulation for only a first period of time that is selected to minimize stress to tissue. As indicated in FIG. **13**, processor **110** of INS **26** may control stimulation generator **114** to deliver the first stimulation therapy to patient until a timer, which defines the first time period, expires (**182**).

The first time period during which the first stimulation therapy is delivered may generally be any amount of time approximately less than or equal to that of the maximum period that INS may deliver neurostimulation according to the first therapy program without stressing tissue. In some example, INS **26** may be pre-programmed with a "safe" time period for a given stimulation parameter value or set of stimulation parameter values based on which the first time period is defined. Additionally or alternatively, INS **26** may be configured such that a physician may define the first time period, e.g., via programmer **24**, to allow for first time period that is tailored to a particular patient. In examples in which the first stimulation therapy includes relatively high intensity stimulation, the first time period may be less than or approximately equal to 1 minute, e.g., less than or approximately equal to 30 seconds.

In any case, once the first time period timer (**182**) has expired, INS **26** may terminate delivery of the first stimulation therapy and initiate delivery of a second stimulation therapy (**184**). The first and second stimulation therapies may be defined by therapy programs stored in memory **112** of INS **26** (FIG. **7**) or a memory of another device. The first and second therapy programs may have at least one different stimulation parameter. In some examples, the second stimulation therapy has a lower intensity than the first stimulation therapy. The stimulation intensity may be a function of the stimulation parameter values, such as the pulse rate, pulse width, duty cycle, amplitude, and the like. In some examples, the second therapy program may have a lower frequency and/or lower stimulation amplitude (e.g., current or voltage amplitude) than the first therapy program. The lower stimulation intensity of the second stimulation therapy may allow for continued delivery of electrical stimulation for a longer period of time compared to the first stimulation therapy without a significant likelihood of causing one or more undesirable side effects. In other cases, the second stimulation therapy may define a period during which INS **26** does not deliver electrical stimulation to the tissue site of patient **12**, effectively ending delivery of electrical stimulation to patient **12** after the expiration of the first time period. In some examples, the intensity of the first and/or second stimulation therapies may be ramped up (e.g., by increasing amplitude or duration of duty cycle) to reduce muscle twitch or pain experienced by patient due to the stimulation.

Similar to that of the first stimulation, the second stimulation therapy may be delivered for a second time period following the first time period. The second time period may be defined by a timer, e.g., similar to that shown in FIG. **13** for defining the first time period for delivery of the first stimulation therapy. In some examples, the second time period may be longer than that of the first time period for the first stimulation therapy, e.g., in cases in which the second stimulation therapy is of a lower intensity than the first therapy thus allowing the second stimulation therapy to be delivered for a longer period of time without a significant likelihood of causing one or more undesirable side effects. Once the second time period has expired, the delivery of the second stimulation therapy from INS **26** to patient **12** may be terminated.

In some examples, upon expiration of the second time period for delivery of second stimulation therapy, INS **26** or other device may determine whether heart **12** is in an EMD state, which can be the same EMD state occurrence as the previously detected EMD state (**178**) or may be a separate occurrence that is, e.g., separated in time from the previous EMD state detection. INS **26** or other device may determine that heart **12** is in the EMD state using one or more the techniques described herein. For examples, INS **26** may sense at least one physiological parameter of patient **12** after delivery of the defibrillation therapy, which may then be used to determine an EMD state of heart **14**, e.g., as described above with respect to FIG. **10**.

If the EMD state of heart **14** is detected after the delivery of the second therapy (**184**), INS **26** may initiate delivery of stimulation therapy to treat the EMD state. In some examples, the stimulation therapy may have the same or similar stimulation parameters as that of the first and/or second stimulation therapies described above with regard to FIG. **13**, while in other examples one or more of the stimulation therapy parameters values may be adjusted from that of the first and/or second stimulation therapies to treat the new EMD state. If INS **26** does not detect an EMD state after the second therapy is terminated, INS **26** may continue to monitor patient **12** to detect if and when heart **14** enters an EMD state so that stimulation may be delivered to treat the EMD state at that time. In such an example, system **10** may monitor and treat patient **12** for occurrences of EMD in a closed-loop manner.

FIG. **14** is a flow diagram illustrating an example technique for delivering electrical stimulation to a patient when a heart of the patient is in an EMD state. As described above, in some examples, a therapy system, such as therapy system **10** or therapy system **80** may be configured to monitor autonomic nervous system activity of patient **12** to determine autonomic nervous system activity associated with an EMD state. For ease of illustration, the example technique of FIG. **14** is described with regard to therapy system **10** but is

not limited in implementation to such therapy system configurations. Moreover, although the example technique of FIG. **14** is primarily described with regard to INS **26**, one or more aspects of the technique may be performed by another device, such as ICD **16**, programmer **24** or ICD **80** either in combination with INS **26** or exclusive from that of INS **26**.

As illustrated in FIG. **14**, processor **110** (FIG. **7**) of INS **26** detects that heart **14** is in an EMD state (**186**), e.g., using one or more of the techniques described herein for detecting that heart **14** is in EMD state. Upon detecting that heart **14** is in an EMD state, processor **110** (FIG. **7**) determines autonomic activity associated with the EMD state of heart **14** (**188**). As discussed above, the autonomic nervous system activity associated with the EMD state of heart **14** can be indicated by the activity level of sympathetic and parasympathetic nervous system activity relative to each other, or just one of the sympathetic or parasympathetic nervous system activities. In addition, the autonomic nervous system activity associated with the EMD state of heart **14** can be the autonomic nervous system activity temporally correlating to the detection of the EMD state by processor **110**, and, in some examples, includes the time period before and/or after detection of the EMD state by processor **110**. A loop recorder or the like can be used to store sensed signals indicative of autonomic nervous system activity (e.g., sensed sympathetic nervous system activity) for the time period before the detection of the EMD state. Processor **110** (FIG. **7**) of INS **26** then controls the delivery of therapy to patient **12** based on the autonomic nervous system activity determined to be associated with the EMD state of heart **14** (**190**).

The monitored autonomic activity of patient **12** analyzed by INS **26** may include sympathetic nervous system activity and/or parasympathetic nervous system activity of patient **12**. For ease of illustration, examples of the disclosure may primarily be described with regard to sympathetic activity. Processor **110** can determine the nerve activity of a sympathetic or parasympathetic nerve using any suitable technique. In some examples, sensing module **119** (FIG. **7**) generates an electrical signal that is indicative of an electrical nerve signal generated by a nerve, such as the target sympathetic or parasympathetic nerve used to determine autonomic nervous system activity or a branch thereof, in response to an electrical stimulation signal delivered by the electrodes of lead **28** or lead **31**. The electrical nerve signal may be sensed between two or more electrodes of lead **28** or lead **31** (FIG. **7**). Processor **110** may analyze the electrical nerve signal for an indication of autonomic nervous system activity, for example, by measuring an amplitude of the electrical nerve signal and comparing the measured value to a threshold value. The threshold value may be, for example, an amplitude or other characteristics of a sensed electrical signal.

Autonomic activity associated with the EMD state of heart **14** may be autonomic activity sensed just prior to or during the occurrence of an EMD state of heart **14**. In some examples, the autonomic activity associated with the EMD state may be an underlying cause of the EMD state of heart **26**. For example, in some cases, heart **14** may be in an EMD state due in part to elevated sympathetic nervous system activity. In other examples, heart **14** may be in an EMD state due in part to decreased sympathetic nervous system activity. By determining the autonomic nervous system activity associated with heart **14** when in an EMD state, processor **110** of INS **26** may control delivery of therapy to address the autonomic activity associated with the EMD state of heart **14** in a manner that effectively treats the EMD state of heart **14**. In particular, processor **110** controls stimulation generator **114** to generate and deliver stimulation therapy to patient **14** that addresses at least one contributing factor to the EMD state. In this way, the therapy delivered by INS **26** is relevant to the particular EMD state of patient **12**.

As an illustration, processor **110** of INS **26** may determine that the autonomic nervous system activity associated with the detected EMD state of heart **26** includes a depressed level of sympathetic activity. Based on the depressed level of sympathetic nervous system activity determined to be associated with the EMD state of heart **14**, processor **110** of INS **26** may control delivery of therapy to patient **12** to increase the level of sympathetic nervous system activity in patient **12**. Such stimulation may effectively treat the detected EMD state of heart **12**, e.g., by promoting mechanical contraction of heart **12**.

In some examples, after delivering stimulation therapy to patient **12** that is configured to increase sympathetic nervous system activity, e.g., when a depressed level of sympathetic nervous system activity is associated with a detected EMD state of heart **14**, INS **26** may subsequently adjust the stimulation therapy to then reduce sympathetic nervous system activity for patient **12**. For example, INS **26** may deliver a first stimulation therapy generated according to a first therapy program that is configured to increase sympathetic activity may be delivered to patient for a first time period. The first time period may be selected to effectively bring heart **14** out of the EMD state with the first stimulation therapy configured to increase sympathetic nervous system activity. Following the expiration of the first time period and the corresponding increase in sympathetic activity of patient **12**, processor **110** of INS **26** may modify the stimulation being delivered to patient **12** to deliver a second stimulation therapy to patient **12** that is configured to decrease sympathetic activity in patient **12**.

In such an example, while the first stimulation therapy may increase the sympathetic activity to a level that effectively brings heart **14** out of the detected EMD state, such a level of sympathetic activity may not be sustainable and/or may lead to undesired side effects. As such, once INS **26** delivers the first therapy to, in essence, increase the contractility of heart **14** and bring heart **14** out of an EMD state by increasing the sympathetic nervous system activity, INS **26** may deliver a second therapy generated according to a second therapy program that reduces sympathetic activity of patient **12**, e.g., to a baseline level or some other level of sympathetic activity to avoid undesired side effects. In some examples, the second stimulation therapy may be delivered to reduce sympathetic activity to be less than that experience by patient due to the first stimulation therapy but greater than the sympathetic activity associated with the EMD state. The first and second therapy programs have at least one different stimulation parameter value.

As another example, in other cases, processor **110** of INS **26** may determine that autonomic activity associated with the detected EMD state of heart **14** includes a relatively high level of sympathetic activity. Upon determining heart **14** is in an EMD state and the EMD state is associated with a relatively high level of sympathetic activity, processor **110** can control stimulation generator **114** to generate and deliver stimulation therapy to patient **12** in a manner that decreases sympathetic activity of patient **12**. Again, such stimulation may effectively treat the detected EMD state of heart **12**, e.g., by promoting mechanical contraction of heart **12**, by decreasing sympathetic nervous system activity from that associated with the EMD state of heart **12**.

As described above, system **10** may monitor autonomic activity of patient **12** using any suitable methodology. In some examples, processor **110** of INS **26** (or a processor of another device such as ICD **16**) may determine autonomic activity of patient **12** by monitoring the electrical activity of heart **14**. As described above, sensing module **96** of ICD **16** may monitor signals from at least one of electrodes **50**, **52**, **54**, **56**, **58**, **60**, **68**, **72**, **74**, and **76** in order to monitor electrical activity of heart **14**, e.g., via an EGM signal. In such an example, processor **110** may receive the sensed electrical activity of heart **14** from ICD **16** and analyze the sensed electrical activity of heart **14** to determine the heart rate of heart **14** and/or heart rate variability (e.g., P-P interval variability and/or R-R interval variability) that may be indicative of autonomic nervous system activity. Alternatively, processor **90** of ICD **16** may make the determination and transmit an indication of the autonomic nervous system activity to processor **110**.

As one example, sympathetic activity of a patient **12** may be monitored and determined by sensing the heart rate of heart **14**. During an EMD state, the heart rate of heart **14** may be determined based on the sensed electrical signals of heart **14** (e.g., an ECG or EGM) despite that fact heart **26** is generally not mechanically contracting in a physiologically significant manner due to the EMD state. Processor **110** of INS **26** (or another processor) can compare the heart rate indicated by the sensed electrical activity of heart **14** during an EMD state or just prior to the occurrence of an EMD state to a threshold value to determine if the heart rate is relatively low, e.g., as compared to an average heart rate of patient **12**. If processor **110** determines that the heart rate is relatively low, processor **110** may determine that the sympathetic activity of patient **12** is depressed. Sensed electrical activity of heart **14** that reflects a relatively low heart rate, such as, e.g., about 20 to 30 beats per minute (BPM) compared to a "normal" heart rate of about 60 to about 70 BPM, may be indicate depressed sympathetic activity. In response to the depressed sympathetic activity, INS **26** (or ICD **16**) may deliver stimulation therapy to patient **12** in a manner that increases sympathetic activity to treat the EMD state of heart.

Conversely, if processor **110** determines that the heart rate indicated by the sensed electrical activity of heart **14** during an EMD state or just prior to the occurrence of an EMD state is relatively high, e.g., as compared to an average heart rate of patient **12** or one or more threshold heart rate values or ranges, processor **110** may determine that the sympathetic activity of patient **12** is overexcited. In some examples, sensed electrical activity of heart **14** that reflects a relatively high heart rate, such as, e.g., about 100 to 120 beats per minute (BPM), may be indicate overexcited sympathetic activity. As described above, in response, INS **26** (or ICD **16**) may deliver stimulation therapy to patient **12** to decrease sympathetic activity to treat the EMD state of heart **14**. The low heart rate, high heart rate, and/or normal heart rate may be predetermined and stored by ICD **16**, INS **26** or another device. In other examples, the normal heart may be determined based on, for example, an average sensed heart rate for a predetermined period of time preceding the detection of the EMD state. In this way, the "normal" heart rate may be a dynamically changing value.

Additionally or alternatively, heart rate variability (e.g., P-P interval variability and/or R-R interval variability) may also be analyzed by processor **110** (or another processor) to monitor and determine autonomic activity to treat the detected EMD state of patient **14**. In some examples, sensed electrical activity of heart **14** that reflects an increase in heart rate variability may indicate overexcited parasympathetic nervous system activity. In this way, heart rate variability may be used as an indicator for the nature of the autonomic nervous system activity associated with a detected EMD state.

As another example, processor **110** of INS **26** (or another device) may determine autonomic activity of patient **12** associated with an EMD state by monitoring electrical nerve activity of patient **12**. For example, sensing module **119** may monitor electrical activity of a nerve (e.g., a vagal nerve) via sensor **121** (FIG. **7**) and generate an electrical signal indicative of the electrical nerve activity. Processor **110** may receive the electrical signal and extract signal characteristic directly from the signal or from a parameterized signal or data generated based on the raw electrical nerve signal in order to determine whether the electrical nerve activity is indicative of an excited or depressed parasympathetic nervous system activity level and/or an excited or depressed sympathetic nervous system activity level.

In such an example, processor **110** (FIG. **7**) may analyze the sensed electrical signal when heart **14** is determined to be in an EMD state. If nerve activity is for the vagus nerve or another parasympathetic nerve and the sensed vagal nerve electrical activity indicates a relatively high amount of vagal nerve activity, then INS **26** may determine that the parasympathetic activity of patient **12** is overexcited. In such a case, the detected EMD state may be caused by vagal nerve overexcitation. Processor **110** can compare a signal characteristic of the electrical nerve signal to a predetermined threshold value (e.g., stored in memory **112**) to determine whether the sensed vagal nerve (or other parasympathetic nerve) electrical activity indicates a relatively high amount of vagal nerve activity. In some examples, processor **110** can supplement the determination by determining whether the heart rate of patient **12** is also relatively low. In response to the vagal overexcitation, processor **110** can controls stimulation generator **114** of INS **26** (or ICD **16**) may deliver stimulation therapy to patient **12** to increase sympathetic activity to treat the EMD state of heart.

Processor **110** can also apply a similar technique to determine whether an electrical nerve signal generated by a sympathetic nerve indicates a relatively high amount of sympathetic activity. For example, processor **110** can compare a signal characteristic of the sensed electrical nerve signal of the sympathetic nerve to a predetermined threshold value (e.g., stored in memory **112**) to determine whether the sensed nerve electrical activity indicates a relatively high amount of sympathetic nervous system activity. Processor **110** can then select the EMD stimulation therapy parameters based on the determination, e.g., by selecting a therapy program from memory **112** or adjusting one or more stimulation parameter values of a particular therapy program.

As another example, processor **110** (or another processor) may determine autonomic activity of patient **12** via intracardiac nerve recording. For example, INS **26** and/or ICD **16** may be configured to monitor electrical activity at the atrioventricular (AV) node. The AV node of patient **12** may include a large number of parasympathetic nerve fibers. As such, electrical activity monitored at the AV node may be used as an indicator of excited or depressed parasympathetic nervous system activity. If ICD **16** senses the electrical activity at the AV node, ICD **16** can transmit an indication of the electrical activity or the raw signal to INS **26** via the respective telemetry modules or another suitable communication technique. In some examples, the stimulation therapy delivered to patient **12** from INS **26** to treat heart **14** when

in an EMD state may be based on the parasympathetic activity indicated by the sensed AV node electrical activity.

Similarly, processor **110** may determine autonomic activity of patient **12** via sympathetic ganglion recording. For example, INS **26** may be configured to monitor electrical activity at one or more sympathetic ganglia of patient **12**. Sympathetic ganglia of patient **12** may include a high number of sympathetic nerve fibers. As such, electrical activity monitored at one or more sympathetic ganglia may be used as an indicator of excited or depressed sympathetic nervous system activity. In some examples, the stimulation therapy delivered to patient **12** from INS **26** to treat heart **14** when in an EMD state may be based on the sympathetic activity indicated by the sensed sympathetic ganglion electrical activity. Additionally or alternatively, in a similar fashion, processor **110** of INS **26** may monitor parasympathetic ganglion electrical activity, e.g., to identify depressed or overexcited parasympathetic activity.

FIG. **15** is a flow diagram illustrating an example technique for delivering stimulation to patient **12** when heart **14** of patient **12** is in an EMD state. Processor **110** of INS **26** or a processor of another device, or a combination of processors of one or more devices, can apply the technique shown in FIG. **15**, such as by executing machine readable instructions that are stored in memory **112**. Processor **110** can apply the technique shown in FIG. **15** to identify autonomic activity associated with a detected EMD state, and control stimulation therapy to treat the EMD state that is configured based on the autonomic nervous system activity associated with the EMD state. For ease of illustration, the example technique of FIG. **15** is described with regard to therapy system **10** but is not limited in implementation to such therapy system configurations. Moreover, although the example technique of FIG. **15** is primarily described with regard to INS **26**, one or more aspects of the technique may be performed by ICD **16**, programmer **24** or ICD **80** either in combination with INS **26** or exclusive from that of INS **26**.

As illustrated in FIG. **15**, INS **26** monitors by the heart rate of patient **12**, which is determined based on electrical activity of heart **14** sensed via sensing module **119** and sensor **121** (**192**). Heart rate can be indicated by, for example, the heart beats per minute (BPM). In other examples, ICD **16** can transmit an indication of the heart rate, e.g., a heart rate value, the raw electrical cardiac signal or a parameterized indication of the electrical cardiac signal to INS **26** via the respective telemetry modules **98**, **118**, and processor **110** can determine the heart rate based on the information received from ICD **16**. Processor **110** can periodically determine the heart rate of patient **12**, e.g., at predetermined intervals of time, or processor **110** can continuously determine heart rate.

While monitoring the heart rate of patient **12**, processor **110** (FIG. **7**) of INS **26** may determine whether heart **14** is in an EMD state (**194**), e.g., using one or more of the techniques described herein for detecting that heart **14** is in EMD state. If processor **110** determines that heart **14** is in an EMD state, processor **110** analyzes a sensed electrical cardiac signal (e.g., EGM or ECG) of patient **12** to determine whether the electrical cardiac signal indicates a relatively low heart rate (**196**). For example, processor **110** may compare the heart rate indicated by the sensed electrical activity to a threshold value or threshold range determined to be indicative of a low heart rate. In one example, processor **110** of INS **26** may classify any heart rate below approximately 30 BPM, such as, between approximately 20 to approximately 30 BPM, as a low heart rate. The threshold value or threshold range can be predetermined and stored in memory **112** (FIG. **7**). In other examples, the threshold value or threshold range can be dynamic and can change based on the historic heart rate of patient **12**. For example, the threshold value that indicates a low heart rate can be a mean, median, or lowest heart rate for a predetermined time range preceding the detection of the EMD state.

If processor **110** determines that the heart rate indicated by the sensed electrical activity is not a "low" heart rate, then processor **110** evaluates one or more indicators of increased sympathetic nervous system activity to determine if the indicators reflect increased or overexcited sympathetic nervous system activity (**198**). As described above, suitable indicators of increased sympathetic activity may include sensed nerve activity and/or heart rate variability. In some examples, processor **119** may analyze the heart rate of patient **12** previously determined to not be a "low" heart rate to determine whether the heart rate indicated by the sensed electrical signals is a relatively high or elevated heart rate. As described above, a "high" heart rate (e.g., a heart rate greater than approximately 100 BPM, such as, approximately 100 to approximately 120 BPM, may be an indicator of increased or overexcited sympathetic nervous system activity. As with determining whether a determined heart rate of patient **12** is low, processor **110** can determine whether the heart rate indicated by the sensed electrical cardiac activity is relatively high by comparing the heart rate to a threshold value or threshold range determined to be indicative of a relatively high heart rate. The threshold value or threshold range can be predetermined and stored in memory **112** (FIG. **7**). In other examples, the threshold value or threshold range can be dynamic and can change based on the historic heart rate of patient **12**. For example, the threshold value that indicates a relatively high heart rate can be a mean, median, or peak heart rate for a predetermined time range preceding the detection of the EMD state.

If processor **110** determines that that the one or more indicators of increased sympathetic activity (**198**) indicate that the EMD state is associated with increased sympathetic nervous system activity, processor **110** controls stimulation generator **114** (FIG. **7**) to generate and deliver electrical stimulation to patient **12** that is configured to decrease sympathetic activity (**206**). In one example, INS **26** delivers electrical stimulation having a pulse rate of approximately 10 Hz to approximately 80 Hz, and a voltage amplitude of approximately 3 volts to approximately 6 volts to one or more target sites to decrease sympathetic activity. Other example stimulation parameter values are contemplated.

If processor **110** determines that the heart rate indicated by the sensed electrical signals is a relatively "low" heart rate, thereby indicating that the detected EMD state may be associated with overexcitation of the parasympathetic nervous system, processor **110** may initially determine that the autonomic nervous system activity associated with the EMD state includes vagal overexcitation or overexcitation of another parasympathetic nerve (**200**). Vagal nerve overexcitation is referenced herein for purposes of example only. Processor **110** may arrive at a similar determination if the indicator of increased sympathetic activity (**198**) does not indicate increased sympathetic nervous system activity after a determination that the heart of patient **12** is not a "low" heart rate. To verify the vagal overexcitation, similar to that described above, processor **110** may analyze one or more monitored parameters that may be used as indicators of overexcited or increased sympathetic activity (**202**). The indicator of increased sympathetic nervous system activity (**202**) may be the same or different from the indicator of

increased sympathetic activity (**198**) analyzed by processor **110** after it was determined that the sensed electrical activity of heart **14** did not indicate a relatively "low" heart rate. In some examples, processor **110** may additionally or alternatively analyze one or more monitored parameters that may be used as indicators of overexcited or increased parasympathetic activity, e.g., to verify detected vagal overexcitation (**200**).

If processor **110** determines that the indicator of increased sympathetic nervous system activity (**202**) reflects increased sympathetic nervous system activity, processor **110** controls stimulation generator **114** to generate and deliver electrical stimulation to patient **12** that is configured to decrease sympathetic activity (**206**). Conversely, if the indicator of sympathetic nervous system activity (**202**) does not reflect increased sympathetic nervous system activity, processor **110** can control stimulation generator **114** to deliver electrical stimulation to patient **12** that is configured to increase sympathetic activity (**204**). In one example, stimulation generator **114**, under the control of processor **110**, generates and delivers electrical stimulation having a frequency (e.g., a pulse rate) of greater than approximately 100 Hz, and a voltage amplitude of approximately 5 volts to approximately 10 volts to one or more target sites to increase sympathetic activity. Other example stimulation parameter values are contemplated. In some examples, this relatively high frequency stimulation may be initially delivery to "wake-up" or bring the heart out of the detected EMD state, e.g., by inducing one or more mechanical contractions. Similar to that described above, after a set period of time, INS **26** can terminate delivery of the high frequency stimulation and deliver a lower intensity stimulation, e.g., to avoid undesirable side-effects from the high intensity stimulation to the same or a different tissue site as the high frequency stimulation.

Whether INS **26** delivers stimulation to decrease sympathetic activity sympathetic activity (**206**) or increase sympathetic activity (**204**) based on the autonomic nervous system activity determined to be associated with the EMD state of heart **14**, after delivery of the stimulation, e.g., for some predetermined time period, processor **110** may determine whether heart **14** is still in an EMD state (**208**). If the delivered stimulation did not terminate the EMD state (e.g., heart **14** is not contracting in a physiologically significant manner), processor **110** may modify one or more stimulation parameter values from the previously delivered stimulation (**212**) and deliver the modified stimulation to patient **12** (**214**). As described above, in some examples, in order to modify the one or more stimulation parameter values to find an effective neurostimulation therapy that terminates the EMD state, processor **110** may be configured to sequentially select a therapy program from a predetermined set of therapy programs, e.g., defining different stimulation signals, electrode combinations, and electrode locations. In some examples, INS **26** may deliver stimulation according to each program for between approximately 5 seconds to approximately 60 seconds, and check whether heart **14** is still in the EMD state after each therapy delivery session with the selected therapy program. If a therapy program is found to be effective in terminating the EMD state, processor **110** can continue to control stimulation generator **114** to generate and deliver therapy according to that therapy program until the EMD state is terminated.

Once the EMD state has been terminated, processor **110** may assess the cardiac and/or autonomic nervous system state of patient **12** (**210**). While the EMD state of patient **12** may be successfully terminated, the cardiac state and/or autonomic state of patient may not have returned to a desirable state, e.g., a state in which the likelihood of a subsequent EMD state is relatively low. For example, the heart rate of patient **12** may be elevated or depressed from that of a desired heart rate. In some examples, the monitored heart rate may display an undesirable level of variability. In some examples, processor **110** may determined that the parasympathetic and/or sympathetic nervous system activity remains depressed or overexcited. Based on the cardiac and autonomic assessment, processor **110** can control stimulation generator **114** to generate and deliver stimulation to manage cardiac and/or autonomic state when determined to be undesirable. As described above, in some examples, INS **26** may continue to delivery therapy to patient **12** for approximately 30 seconds to approximately 120 minutes after the EMD state has been terminated as a follow-up therapy to help assure that EMD state does not imminently reappear. The stimulation therapy delivered by INS **26** can initiate at a relatively large amplitude or duty cycle "on" time to treat an EMD state. Then, after EMD is resolved, the stimulation therapy may be adjusted, e.g., to remain at a relatively lower amplitude and/or duty cycle or even deactivated.

In some aspects, examples of the disclosure may include a method comprising determining whether a heart of a patient is in an electromechanical dissociation state; determining autonomic nervous system activity of the patient associated with the electromechanical dissociation state; and delivering electrical stimulation to the patient based on the determined autonomic nervous system activity of the patient associated with the electromechanical dissociation state.

In one example, determining the autonomic nervous system activity of the patient comprises at least one of determining whether sympathetic nervous system activity of the patient is overexcited or depressed, or determining whether parasympathetic nervous system activity of the patient is overexcited or depressed.

In one example, the example method further comprising delivering first electrical stimulation therapy to the patient to increase sympathetic nervous system activity upon determining that the heart is in the electromechanical dissociation state, wherein delivering electrical stimulation to the patient based on the determined autonomic activity level comprises delivering second electrical stimulation therapy to the patient based on the determined autonomic activity after delivery of the first electrical stimulation. In some examples, the first electrical stimulation has a frequency greater than approximately 100 hertz. In some examples, the second electrical stimulation therapy is configured to reduce sympathetic nervous system activity.

In one example, determining autonomic activity of the patient comprising detecting overexcited sympathetic nervous system activity of the patient, and wherein delivering electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state comprises delivering electrical stimulation configured to decrease sympathetic nervous system activity to the patient.

In one example, determining autonomic activity of the patient comprising detecting depressed sympathetic nervous system activity of the patient, and wherein delivering electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state comprises delivering electrical stimulation configured to increase sympathetic nervous system activity to the patient.

In one example, determining the autonomic nervous system activity of the patient comprises determining the autonomic nervous system activity of the patient based on at least one of sensed electrical activity of the heart or sensed electrical nerve activity.

In one example, determining whether the heart of the patient is in the electromechanical dissociation state comprises determining whether the heart of the patient is in the electromechanical dissociation state based on the at least one sensed physiological parameter. In some examples, the at least one physiological parameter of the patient comprises one or more parameters indicative of mechanical contraction of the heart.

In some aspects, examples of the disclosure may include a medical system comprising a stimulation generator and a processor. The processor determines whether a heart of a patient is in an electrical mechanical dissociation state, determines autonomic nervous system activity of the patient associated with the electromechanical dissociation state, and controls the stimulation generator to deliver electrical stimulation to the patient based on the determined autonomic nervous system activity of the patient associated with the electromechanical dissociation state.

In one example, the processor determines the autonomic nervous system activity of the patient by at least one of determining whether sympathetic nervous system activity of the patient is overexcited or depressed, or determining whether parasympathetic nervous system activity of the patient is overexcited or depressed.

In one example, the processor controls the stimulation generator to deliver first electrical stimulation therapy to the patient to increase sympathetic nervous system activity upon determining that the heart is in the electromechanical dissociation state, and subsequently controls the stimulation generator to deliver the electrical stimulation to the patient based on the determined autonomic activity level by delivering second electrical stimulation therapy to the patient based on the determined autonomic activity after the delivery of the first electrical stimulation. In some examples, the first electrical stimulation comprises a frequency greater than approximately 100 hertz. In some examples, the second electrical stimulation therapy delivered to the patient is configured to reduce sympathetic nervous system activity.

In one example, the processor determines autonomic activity of the patient by at least detecting overexcited sympathetic nervous system activity of the patient, and wherein the processor controls the stimulation generator to deliver electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state by at least delivering electrical stimulation configured to decrease sympathetic nervous system activity to the patient.

In one example, the processor determines autonomic activity of the patient by at least detecting depressed sympathetic nervous system activity of the patient, and wherein the processor controls the stimulation generator to deliver electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state by at least delivering electrical stimulation configured to increase sympathetic nervous system activity to the patient.

In one example, the medical system further comprises a sensor that senses at least one of electrical activity of the heart or electrical nerve activity, wherein the processor determines the autonomic activity of the patient based on at least one of the sensed electrical activity of the heart or the sensed electrical nerve activity.

In one example, the medical system further comprises a sensor that senses at least one physiological parameter of the patient indicative of mechanical contraction of the heart, wherein the processor determines whether the heart of the patient is in an electrical mechanical dissociation state based on the at least one sensed physiological parameter of the patient,

In some aspects, examples of the disclosure may include a medical system comprising means for determining whether a heart of a patient is in an electromechanical dissociation state; means for determining autonomic activity of the patient associated with the electromechanical dissociation state; and means for delivering electrical stimulation to the patient based on the determined autonomic activity of the patient associated with the electromechanical dissociation state.

In one example, the means for determining the autonomic nervous system activity of the patient comprises at least one of means for determining whether the sympathetic nervous system activity of the patient is overexcited or depressed, or means for determining whether the parasympathetic nervous system activity of the patient is overexcited or depressed.

In some aspects, examples of the disclosure may include a method of treating an electromechanical disassociation state of a heart of a patient, wherein the method is characterized by implanting a medical device system in a patient, where the medical device system comprises a stimulation generator, and a processor that determines whether a heart of a patient is in an electrical mechanical dissociation state, determines autonomic nervous system activity of the patient associated with the electromechanical dissociation state upon determining that the heart is in the electromechanical dissociation state, and controls the stimulation generator to deliver electrical stimulation to the patient based on the determined autonomic nervous system activity of the patient associated with the electromechanical dissociation state.

In one example, the medical device system further comprise a sensor that generate a signal indicative of the at least one physiological parameter of the patient indicative of mechanical contraction of the heart, wherein the processor determines whether the heart of the patient is in the electrical mechanical dissociation state based on the signal.

Although the examples provided are primarily described with respect to implantable medical devices and systems, examples are not limited as such. In some examples, one or more of the described techniques may be incorporated into an external device, such as, e.g., as external defibrillator, to determine if a patient's heart is in an EMD state and provide therapy to patient based on the determination. In such cases, electrical stimulation may be provided to a patient via one or more external electrodes positioned proximate an appropriate tissue site of the patient to treat the EMD state as described herein.

The techniques described in this disclosure, including those attributed to ICD **16**, INS **26**, programmer **24**, ICD **82** or various constituent components, may be implemented, at least in part, in hardware, software, firmware or any combination thereof. For example, various aspects of the techniques may be implemented within one or more processors, including one or more microprocessors, DSPs, ASICs, FPGAs, or any other equivalent integrated or discrete logic circuitry, as well as any combinations of such components, embodied in programmers, such as physician or patient programmers, stimulators, image processing devices or other devices. The term "processor" or "processing circuitry" may generally refer to any of the foregoing logic

circuitry, alone or in combination with other logic circuitry, or any other equivalent circuitry.

Such hardware, software, firmware may be implemented within the same device or within separate devices to support the various operations and functions described in this disclosure. While the techniques described herein are primarily described as being performed by processor **90** of ICD **16**, processor **110** of INS **26**, and/or processor **130** of programmer **24**, any one or more parts of the techniques described herein may be implemented by a processor of one of the devices **16**, **26**, programmer **24** or another computing device, alone or in combination with ICD **16**, INS **26** or programmer **24**.

In addition, any of the described units, modules or components may be implemented together or separately as discrete but interoperable logic devices. Depiction of different features as modules or units is intended to highlight different functional aspects and does not necessarily imply that such modules or units must be realized by separate hardware or software components. Rather, functionality associated with one or more modules or units may be performed by separate hardware or software components, or integrated within common or separate hardware or software components.

When implemented in software, the functionality ascribed to the systems, devices and techniques described in this disclosure may be embodied as instructions on a computer-readable medium such as RAM, ROM, NVRAM, EEPROM, FLASH memory, magnetic data storage media, optical data storage media, or the like. The instructions may be executed to support one or more aspects of the functionality described in this disclosure.

Various examples of the disclosure have been described. These and other examples are within the scope of the following claims.

The invention claimed is:

1. A method comprising:

sensing at least one physiological parameter of a patient;

determining whether a heart of the patient is in an electromechanical dissociation state based on the at least one sensed physiological parameter; and

delivering electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electromechanical dissociation state,

wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

2. The method of claim **1**, wherein the tissue site comprises at least one of an efferent nerve site or an afferent nerve site.

3. The method of claim **1**, wherein the tissue site comprises a spinal cord of the patient.

4. The method of claim **1**, wherein the tissue site comprises a tissue proximate to one or more thoracic segments.

5. The method of claim **1**, wherein delivering electrical stimulation to the tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electromechanical dissociation state comprises delivering electrical stimulation to the tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity but not excite efferent nerve activity upon determining that the heart is in the electromechanical dissociation state.

6. The method of claim **1**, further comprising withholding delivery of electrical stimulation to the tissue site when the electromechanical dissociation state is not determined.

7. The method of claim **1**, wherein the at least one physiological parameter of the patient comprises one or more parameters indicative of mechanical contraction of the heart.

8. The method of claim **7**, wherein the at least one physiological parameter comprises at least one of blood pressure, blood flow, respiratory rate, tissue perfusion, pulsatility, blood oxygen concentration, blood sugar concentration, blood pH or blood calcium concentration.

9. The method of claim **1**, wherein determining whether the heart of the patient is in the electromechanical dissociation state comprises comparing the at least one physiological parameter of the patient to a threshold value that is indicative of the electromechanical dissociation state.

10. The method of claim **1**, further comprising sensing delivery of at least one of cardioversion or defibrillation therapy to the heart, wherein delivering electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electromechanical dissociation state comprises delivering the electrical stimulation within approximately 10 seconds of the delivery of the at least one of cardioversion or defibrillation therapy to the heart.

11. The method of claim **1**, wherein delivering electrical stimulation to a tissue site of the patient comprises delivering relatively high frequency electrical stimulation to the tissue site for a first time period and then delivering relatively low frequency electrical stimulation to the tissue site for a second time period, wherein the first time period begins before the second time period.

12. The method of claim **11**, wherein the high frequency electrical stimulation has a frequency in a range of approximately 50 hertz to approximately 100 hertz.

13. The method of claim **11**, wherein the first time period is less than or approximately equal to one minute but greater than zero.

14. A medical system comprising:

a sensor that senses at least one physiological parameter of a patient;

a stimulation generator; and

a processor that determines whether a heart of the patient is in an electrical mechanical dissociation state based on the at least one sensed physiological parameter and controls the stimulation generator to deliver electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

15. The medical system of claim **14**, wherein the tissue site comprises at least one of an efferent nerve site or an afferent nerve site.

16. The medical system of claim **14**, wherein the processor controls the stimulation generator to deliver electrical stimulation to the tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity but not excite efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state.

17. The medical system of claim **14**, wherein the processor controls the stimulation generator to withhold delivery of

electrical stimulation to the tissue site when the electromechanical dissociation state is not determined.

18. The medical system of claim **14**, wherein the at least one physiological parameter of the patient is indicative of mechanical contraction of the heart.

19. The medical system of claim **14**, wherein the at least one physiological parameter comprises at least one of blood pressure or blood flow, respiratory rate, tissue perfusion, pulsatility, blood oxygen concentration, blood sugar concentration, blood pH, or blood calcium concentration.

20. The medical system of claim **14**, wherein the processor determines whether the heart is in the electromechanical dissociation state based at least in part on a comparison of the at least one physiological parameter of the patient to a threshold value.

21. The medical system of claim **14**, wherein the stimulation generator comprises a first stimulation generator, the system further comprising a second stimulation generator that delivers at least one of cardioversion or defibrillation therapy to the heart of the patient, wherein the processor controls the first stimulation generator deliver electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity within approximately 10 seconds of delivery of the at least one of cardioversion or defibrillation therapy to the heart by the second stimulation generator.

22. The medical system of claim **14**, wherein the processor controls the stimulation generator to generate and deliver a relatively high frequency electrical stimulation delivered to the tissue site for a first time period immediately following a determination that the heart is in the electromechanical disassociation state and deliver a relatively low frequency electrical stimulation delivered to the tissue site for a second time period, wherein the first time period begins before the second time period.

23. The medical system of claim **22**, wherein the high frequency electrical stimulation has a frequency between approximately 50 hertz to approximately 100 hertz.

24. A medical system comprising:

means for sensing at least one physiological parameter of a patient;

means for determining whether a heart of the patient is in an electrical mechanical dissociation state of a heart of the patient based on the at least one sensed physiological parameter; and

means for delivering electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state,

wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

25. The medical system of claim **24**, wherein the means for delivering electrical stimulation to the tissue site delivers a relatively high frequency electrical stimulation delivered to the tissue site for a first time period immediately following a determination that the heart is in the electromechanical disassociation state and delivers a relatively low frequency electrical stimulation delivered to the tissue site for a second time period, wherein the first time period begins before the second time period.

26. A method of treating an electromechanical disassociation state of a heart of a patient, wherein the method is characterized by implanting a medical device system in a patient, where the medical device system comprises a stimulation generator and a processor that determines whether the heart of the patient is in the electrical mechanical dissociation state based on at least one sensed physiological parameter and controls the stimulation generator to deliver electrical stimulation to a tissue site of the patient to at least one of modulate afferent nerve activity or inhibit efferent nerve activity upon determining that the heart is in the electrical mechanical dissociation state, wherein the tissue site comprises at least one of a nonmyocardial tissue site or a nonvascular cardiac tissue site.

27. The method of claim **26**, wherein the medical device system further comprise a sensor that generate a signal indicative of the at least one physiological parameter of the patient, wherein the processor determines whether the heart of the patient is in the electrical mechanical dissociation state based on the signal.

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